

*August 2011*

## NIEHS Spotlight



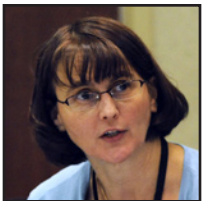
### [NIH-funded research network to explore oil spill health effects](#)

Newly funded research, led by NIEHS, will concentrate on the range of acute and long-term health effects on the general public from the Deepwater Horizon disaster.



### [NIEHS hosts lecture series from scientific director final four](#)

NIEHS presented a four-part lecture series, between June 28 and July 6, of presentations by finalists in the search for its next scientific director.



### [NIEHS takes next step in strategic planning](#)

NIEHS kicked off an intensive three-day stakeholder community workshop July 12 at the Sheraton Imperial Hotel in Research Triangle Park, N.C.



### [Interns enjoy program of career narratives](#)

As part of the NIEHS Summer Internship Program five panelists gathered June 23 to describe their career pathways and experiences in biomedical research.



### [Research fellow joins faculty at the University of South Carolina](#)

Research Fellow Minsub Shim, Ph.D., spent the last eight years in the NIEHS Eicosanoid Biochemistry Group headed by Principal Investigator Thomas Eling, Ph.D.

## Science Notebook



### [NIEHS celebrates five years of ONES research](#)

NIEHS hosted talks on cutting-edge research July 18-19 by 26 of its New Outstanding Environmental Scientists from the years 2006 to 2010.



### [Symposium highlights emerging role of 3D tissue modeling in EHS](#)

Organs-on-a-chip are developing rapidly, and the field appears to be poised for translation into a variety of applications in toxicology, pharmacology, and medicine.



### [Using nutrition to alter host susceptibility to environmental toxicants](#)

Nutritional toxicologist Bernhard Hennig, Ph.D., offered a compelling argument for using nutritional modulation of environmental insults in vasculature-related diseases.



### [Study links phthalate and BPA exposure to altered thyroid signaling in humans](#)

A new study by NIEHS grantees has uncovered strong evidence that increased exposure to chemicals found in plastics could lead to irregular thyroid signaling in humans.

## NIEHS Spotlight



### [Fellows fare well in 2012 award competition](#)

NIEHS excelled once again during the 2012 NIH Fellows Award for Research Excellence competition, with NIEHS trainees receiving 21 of the prestigious awards.



### [NTP fellow wins travel award](#)

Mamta Behl, Ph.D., received a \$1,000 travel award from the Society of Toxicologic Pathology to attend the annual meeting held June 19-23 in Denver.



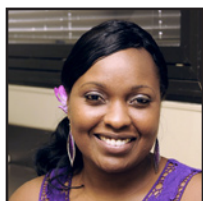
### [NTP postdocs pass laboratory animal medicine boards](#)

NTP postdoctoral fellows Jacquelyn (Jai) Tubbs, D.V.M., and Coralie Zegre-Cannon, D.V.M., learned in July that they've taken an important step in their careers.



### [Henry and Thigpen Tart accepted in leadership program](#)

Two NIEHS employees, Heather Henry, Ph.D., and Kimberly Thigpen Tart, J.D., will be a part of the inaugural NIH Mid-Level Leadership Program in fiscal year 2012.



### [Former NIEHS trainee to spearhead expansion of cancer registry](#)

Tonia Hermon, Ph.D., prepares to return home to the U.S. Virgin Islands where she'll begin a new phase in her professional life.



### [Mutation cluster discovery wins postdoc Roberts a poster prize](#)

NIEHS postdoctoral fellow Steven Roberts, Ph.D., took home a best poster award from the 2011 Gordon Research Conference on Genetic Toxicology.

## Science Notebook



### [Journal features Jean Harry article](#)

The journal *Brain, Behavior, and Immunity* will issue a press release that highlights an article by Jean Harry, Ph.D., and members of her group.



### [NIEHS investigators discover new mechanism in learning and memory](#)

New findings suggest that the timing of neurotransmitter acetylcholine release may play a key role in regulating the strength of nerve cell connections, called synapses.



### [New study explores the unexpected interface of RNA and DNA](#)



A group of NIEHS researchers, led by Thomas Kunkel, Ph.D., was intrigued by the implications of having ribonucleotides involved in DNA replication stability.



### [New journal makes surprising impact in first year of publication](#)

A cross-disciplinary journal with ties to a program funded by NIEHS since 1992 has achieved one of the highest impact factors of specialized journals of its type at 3.592.



### [Ribonucleotide incorporation into DNA study honored by JBC](#)

Research by NIEHS structural biologists provides the latest chapter in the story of a rapidly growing field that investigates the role of ribonucleotide incorporation into DNA.

## NIEHS Spotlight



### [Neurobiologist McPherson wins travel award to meeting in Athens](#)

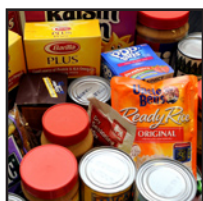
NIEHS Technician Chris McPherson will present research at the 23rd biennial meeting of International Society for Neurochemistry and the European Society for Neurochemistry.



### [Jung honored with mentoring award](#)

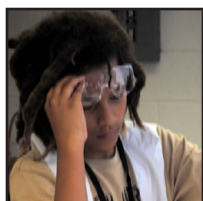
Paul Jung, M.D., was honored June 22 with the U.S. Public Health Service Asian Pacific American Officers Committee RADM Samuel Lin Award.

## Inside the Institute



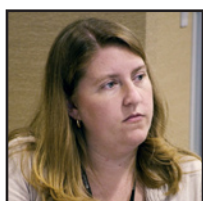
### [Feds Feed Families off to a great start at NIEHS](#)

If the first two drop-box collections June 28-30 and July 27 are any indication, NIEHS is poised to set new records for food donations in 2011.



### [Future scientists are exposed to everyday chemistry](#)

NIEHS scientists and staff volunteered their time and expertise to show the youth of the area that chemistry is everywhere, during a science education program June 25.



### [NIEHS and NIH personnel unite for disabilities awareness](#)

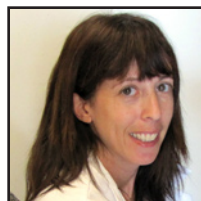
NIH officials hosted an innovative new seminar June 22 at NIEHS designed to promote disabilities awareness and better understanding of accommodation.



### [Students from Duke summer program tour NIEHS](#)

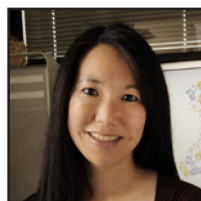
A group of 18 rising seniors and their three graduate student mentors learned about environmental health science during a visit to NIEHS June 18.

## Science Notebook



### [Study finds BPA-exposed male deer mice less attractive to females](#)

A new study led by NIEHS-funded investigators adds fuel to the debate surrounding the safety of products made with the chemical bisphenol A.



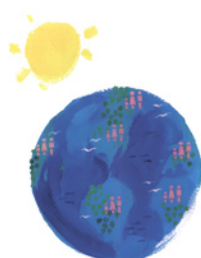
### [Designing a human RNA-binding domain outlined in JBC paper of the week](#)

Structural biologist Tracy Hall, Ph.D., studies RNA-binding domains in gene regulation for insight into how the environment impacts human health.



### [Interns participate in a series of scientific presentations](#)

NIEHS Summer Internship Program participants attended four scientific presentations in June and July to complement their bench training experience this summer.



### [Committee recommends alternative method for product safety testing](#)

In July, an interagency committee transmitted recommendations to federal agencies for using alternative methods in product safety testing.



### [This month in EHP](#)

The August issue of EHP highlights new research into how microbiomes might serve as intermediaries in the process of environmental exposure and affect host susceptibility.



## Calendar of Upcoming Events

- **Aug. 2**, in the Executive Conference Room, 12:00-1:00 p.m. — Receptor Mechanisms Discussion Group presentation on “The metabolic regulator ERRα, a downstream target of HER2/IGF-1, as a therapeutic target in breast cancer,” featuring Ching-Yi Chang, Ph.D.
- **Aug. 2-3**, in Rodbell Auditorium, 8:30 a.m.-4:00 p.m. — Environmental Health Perspectives-sponsored teacher workshops
- **Aug. 4**, in Rodbell C, 10:00-11:00 a.m. — Seminar on “Whole Genome Analysis and Discovery in Cancer,” featuring Elaine Mardis, Ph.D.
- **Aug. 4**, in Rall F193, 11:00 a.m.-12:00 p.m. — Laboratory of Toxicology and Pharmacology Seminar Series presentation by Jean Harry, Ph.D., on “Microglia: Staging of the Inflammatory Response with Hippocampal Injury and Repair”
- **Aug. 16**, in Rall D350, 9:00-11:00 a.m. — CLC Main WorkBench for Sequence Analysis Training
- **Aug. 16**, in Rall D350, 11:00 a.m.-4:30 p.m. — CLC Bio Genomics Software Training
- **Aug. 16**, [online](#), 1:00-2:00 p.m. — Superfund Research Program Trainee Webinar Series, featuring Steven O’Connell and Lucia Rodriguez Freire, Ph.D.
- **Aug. 31**, in Keystone 1003AB, 1:00-2:00 p.m. — Keystone Science Lecture Seminar Series, featuring Leona Samson, Ph.D., topic TBA
- View More Events: [NIEHS Public Calendar](#)

## Extramural Research

### [Extramural papers of the month](#)

- [Some BPA-free bottles live up to their claim](#)
- [Genetic link determined for prostate cancer in African-American men](#)
- [Caffeine and UVB damage](#)
- [Prostate cancer risk increased with ambient exposure to pesticides](#)

## Intramural Research

### [Intramural papers of the month](#)

- [The importance of mechanical stretch in lung epithelial injury](#)
- [NIEHS study investigates the impact of poised RNA polymerase II on neuronal gene transcription](#)
- [Expanded DNA methylation analysis reveals new functional sequences of the genome](#)
- [The regulation of survivin expression in UVB-exposed mouse skin](#)



## NIH-funded research network to explore oil spill health effects

By Ed Kang

An NIH-funded network of researchers will evaluate potential harmful effects of the Deepwater Horizon disaster on reproduction and birth outcomes, the cardiorespiratory system, and behavior and mental health. NIEHS announced the new grant awards in a [press release](#) issued July 7.

The network of community and university partnerships, under the leadership of NIEHS, will conduct research to evaluate the level of potentially harmful contaminants in air, water, and seafood, and assess their relationship to health outcomes.

The five-year, \$25.2 million program will support population-based and laboratory research at Louisiana State University Health Sciences Center, New Orleans; Tulane University, New Orleans; the University of Florida, Gainesville; and The University of Texas Medical Branch at Galveston. In contrast to the NIEHS [GuLF STUDY \(Gulf Long-term Follow-up Study\)](#), which is focused on the oil spill cleanup workers and volunteers, this new research will concentrate on the range of acute and long-term health effects on the general public.

### Program to focus on community health and resiliency in Gulf region

As an integrated network, these four institutions will collaborate on approaches and share results to better understand the interplay and effects of multiple stressors on human health. To ensure research activities are responsive to the needs of local communities in the Gulf Coast region, the universities will partner with more than a dozen community organizations to incorporate local concerns and more effectively communicate research findings.

“From individuals, to families, to communities, this initiative shows a commitment to better understand the long-term health effects of oil spills,” said Linda Birnbaum, Ph.D., director of NIEHS/NTP. “Our number one goal is to provide strong science that will help people now and during future disasters.”

“Throughout the Gulf region, scientists and community groups will work hand in hand to address the needs of those most impacted,” said Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training (DERT), which will closely monitor the progress of the research components. “A focus will be on the physical



*Birnbaum led NIEHS/NTP efforts in the Gulf in the immediate aftermath of the spill, and, under her leadership, NIEHS and NTP have made long-term commitments to the people of the region. (Photo courtesy of Steve McCaw)*



*Collman oversaw the NIEHS cleanup training initiative carried out by the Institute's Worker Education and Training Program, directed by Chip Hughes. DERT is managing oil-spill related grants and efforts by the NIEHS Superfund Research Program. (Photo courtesy of Steve McCaw)*

and psychological health of vulnerable populations, especially pregnant women, children, fishermen, immigrants, and minorities.”

In addition to sharing data and research results, each of the four institutions will implement a community resilience project, which seeks to better understand how local populations respond to, and recover from, disasters. Through their partnerships with community-based organizations, researchers will assess how culture, social networks, and other determinants may enhance pre-event preparedness and post-event recovery.

“This region has seen its share of disasters, and many communities have shown remarkable resilience,” said Claudia Thompson, Ph.D., chief of the Susceptibility and Population Health Branch (SPHB) at NIEHS. “One goal of the research projects is to understand what keeps these communities together, so that other communities can benefit.”

### **A trans-NIH initiative**

In addition to NIEHS, many other NIH components are contributing support to the program, including the National Cancer Institute; National Center for Research Resources; National Heart, Lung, and Blood Institute; National Institute of Mental Health; National Institute on Minority Health and Health Disparities; National Institute of Nursing Research; and the Office of Behavioral and Social Sciences Research. Of the \$25.2 million in total funding, \$3.2 million was provided by BP to NIH specifically for research on the health of Gulf area communities following the oil spill, although BP is not involved in the program or any of its research.

Since the Deepwater Horizon explosion, NIEHS has maintained a continuous and ongoing presence in the Gulf oil spill recovery effort. NIEHS spearheaded efforts to train more than 140,000 cleanup workers through its Worker Education and Training Program. Also, NIEHS is currently leading the GuLF STUDY, the largest health study of its kind ever conducted among cleanup workers and volunteers. The GuLF STUDY has been developed to last up to 10 years and evaluate the health of 55,000 people.

(Ed Kang is a public affairs specialist in the Office of Communications and Public Liaison, and a regular contributor to the Environmental Factor.)

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*Thompson, shown at a recent NIEHS Superfund Research Program talk, and SPHB staff are responsible for direct administration of the new grants. (Photo courtesy of Steve McCaw)*

## **Components of the new research network**

The project titles, universities, and principal investigators (PI) are:

- Women and Their Children’s Gulf Health Consortium — Louisiana State University Health Sciences Center New Orleans, PI Edward Trapido, Sc.D.
- Trans-disciplinary Research Consortium for Gulf Resilience on Women’s Health, — Tulane University, PI Maureen Lichtveld, M.D.
- Health Impact of Deepwater Horizon Spill in Eastern Gulf Coast Communities — University of Florida, PI J. Glenn Morris Jr., M.D.
- Gulf Coast Health Alliance: Health Risks Related to the Macondo Spill — The University of Texas Medical Branch at Galveston, PI Cornelis Elferink, Ph.D.



# NIEHS hosts lecture series from scientific director final four

*By Ian Thomas*

NIEHS presented a four-part lecture series, between June 28 and July 6, of presentations by finalists in the search for its next scientific director. Each presentation was hosted by NIEHS/NTP Director Linda Birnbaum, Ph.D.

Among the Institute's senior leadership posts, this position's primary function involves the leadership and management of the NIEHS Division of Intramural Research (DIR). Comprised of four major programs, 11 laboratories, numerous scientific interest groups, and an annual budget of more than \$100 million, this field-leading investigative body is recognized worldwide for its long-term, high-risk research across a wide array of environmental sciences.

## Meet the Candidates

### Steven Zeisel, M.D., Ph.D.

Currently serving as the Director of the Nutrition Research Institute at the University of North Carolina at Chapel Hill, Zeisel boasts a strong background in both the medical and academic fields. Holding a Ph.D. in nutrition from the Massachusetts Institute of Technology and an M.D. from Harvard University, this renowned expert in metabolic research firmly believes that, for all of its past achievements and accolades, the key to DIR's future success ultimately rests on the innovative spirit and disciplinary diversity of the scientists who comprise it.

"Most major discoveries occur at the boundaries between disciplines when people who know very different things come together for a common goal," Zeisel said of his plan to offer entrepreneurial style incentives to promote bold new cross-disciplinary research. "In combination, they find a way of seeing what was invisible to everyone else."

### Sadis Matalon, Ph.D., Dr. Sc. (Hon)

A leading researcher in the field of pulmonary injury and an NIEHS grantee, Matalon's latest research studies the effects of chlorine exposure on the human respiratory system. Currently the vice chairman of research for the Department of Anesthesiology at the University of Alabama at Birmingham, he reported that ordinary antioxidants such as vitamin C have shown promise for countering the toxic effects of chlorine. Matalon was quick to attribute much of the project's success to the commitment of his research team.



*As host of the talks, Birnbaum, above, did more than stand and wait, as she helped field questions from the audience. (Photo courtesy of Steve McCaw)*



*Zeisel fields questions about his presentation, titled "Metabolic Individuality May Underlie Differences in Responses to Environmental Exposures." He presented the Hans L. Falk Memorial Lecture at NIEHS in October 2010. (Photo courtesy of Steve McCaw)*



“It’s very important to involve people as much as possible and listen to their opinions,” explained Matalon. “Obviously, you won’t always agree on everything but, at the end of the day, people feel vested in the overall goal when they feel as though they’ve contributed something toward achieving it.”

#### Darryl Zeldin, M.D.

Zeldin currently serves as DIR’s acting clinical director and a principal investigator with the NIEHS Laboratory of Respiratory Biology. Boasting an extensive research resume with topics ranging from indoor allergens and asthma to the role of cyclooxygenases in lung and heart function, this graduate of Boston University who earned his M.D. at the Indiana University School of Medicine sees his established track record of success with NIEHS, as well as his abilities to lead and make tough financial decisions in today’s tight economic climate, as being highly beneficial to DIR’s long-term vision moving forward.

“As a leader, it’s always important to keep an eye on the big picture,” he emphasized. “At the same time, a good leader isn’t afraid to get into the weeds of some issues, like the budget for instance, in order to better understand the details of the situation.”

#### David Peden, M.D.

A leader in the field of asthma and lung biology, Peden earned an M.D. from the West Virginia University, and an M.S. in Pharmacology and Toxicology. Presently the director of the Center for Environmental Medicine, Asthma, and Lung Biology at the University of North Carolina at Chapel Hill, he also serves as a professor of pediatrics, in addition to serving as the deputy director for Child Health Research of the NIH Clinical and Translational Science Award consortium at UNC. Still, Peden admits that the notion of vacating his posts to head an organization the size of DIR is incredibly appealing.

“This agency has a wealth of skill sets and personnel experience to offer,” said Peden, an NIEHS grantee for his work on the effects of air pollutants on persons with lung disease. “Bringing those people together creates a real opportunity to investigate new ideas and develop data that will actually influence policy.”

The position of scientific director is central to the mission of the NIEHS, which seeks to reduce the burden of human illness and disability by understanding how the environment influences the development and progression of human disease.

(Ian Thomas is a writer/editor in the NIEHS Office of Communication and Public Liaison)



*Matalon, above, is the principal investigator on two NIEHS grants, “Prevention and Treatment of Chlorine Gas Induced Injury to the Pulmonary System” and “Novel Treatments of Chlorine Induced Injury to the Cardio-Respiratory Systems.” (Photo courtesy of Steve McCaw)*



*Zeldin, whose experience spans the realms of basic and clinical research, focused his presentation, titled “My Vision for Leading the Division of Intramural Research,” on the challenges ahead for DIR. (Photo courtesy of Steve McCaw)*



*Peden, who pointed to several collaborations with NIEHS investigators, is the principal investigator on the NIEHS grant, “Investigating gene x environment interaction using human exposures to O<sub>3</sub> & LPS.” (Photo courtesy of Steve McCaw)*



*Although the lecture series took place over a six-day period, attendance was good right up to the final talk. Many more employees watched the webcast of the talks at their desks or off-site. (Photo courtesy of Steve McCaw)*



*Seated on the front row, NIEHS Principal Investigator Mike Resnick, Ph.D., left, pondered a comment from Acting Scientific Director David Miller, Ph.D., right. Behind them, Office of Policy, Planning, and Evaluation Director Sheila Newton, Ph.D., center, Chief of Staff Paul Jung, left rear, and Deputy Director Rick Woychik, right rear, listened to the speaker. (Photo courtesy of Steve McCaw)*



*People from other divisions, such as Division of the National Toxicology Program scientists Nigel Walker, Ph.D., left, and Ray Tice, Ph.D., right, were also interested in hearing from the people who might be their new colleague. (Photo courtesy of Steve McCaw)*

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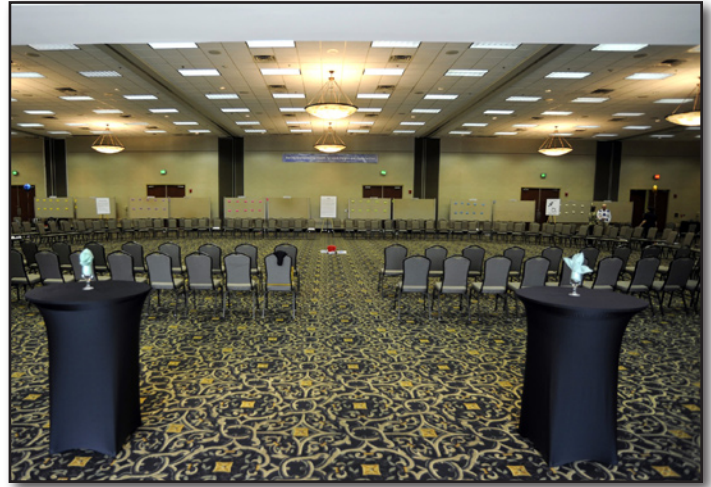


# NIEHS takes next step in strategic planning

By Eddy Ball

NIEHS kicked off an intensive three-day stakeholder community workshop at 1:00 p.m. July 12 at the Sheraton Imperial Hotel and Imperial Conference Center in Research Triangle Park, N.C. More than 170 NIEHS employees, grantees, and scientists from academia, industry, other NIH institutes and centers, the U.S. Food and Drug Administration, and the U.S. Environmental Protection Agency, as well as representatives of community groups with an interest in environmental science and public health, gathered to help shape the [NIEHS Strategic Plan](#) for 2012-2017.

The setting was a massive room at the Sheraton, where the diverse group of attendees began their work seated in a large plenary circle. Along one side of the long room was an agenda wall, with six sets of boards for posting topics participants were passionate about for the future direction of NIEHS. On opposite sides of the common circle were smaller circles where participants convened in groups to discuss and debate more than 100 topics.



*The seating arrangements in the cavernous open space helped promote a sense of equality among participants, by stripping them of furniture, such as desks and tables that can separate people and confer rank. Organizers deliberately omitted titles and academic degrees from nametags for the event. (Photo courtesy of Steve McCaw)*

## Workshop guidelines

NIEHS/NTP Director Linda Birnbaum, Ph.D., set the tone of the workshop with her welcome.

Using a bit of dramatic presentation to focus participants on the greater good, rather than individual interests and goals, Birnbaum put on and removed a series of interesting looking hats as she said, “There’re just different hats, hats we need to make sure we all take off,” in the interest of envisioning future directions for the Institute from the perspective of one NIEHS. “The concept of one NIEHS means that all individual components interact with each other to carry out our central mission over the next five years ... [because] you’re all a part of NIEHS.”

Facilitator Birgitt Williams of Dalar International Consultancy asked participants to check their sense of rank and hierarchy, along with their hats, at the door and engage one another with a sense of respect for the legitimacy of other opinions and other perspectives. Williams explained the four principles of the modified [Open Space Technology](#) format: whoever comes to the discussion are the right people; whenever the discourse starts, it’s the right time; whatever happens is the only thing that could have happened; and, when it’s over, it’s over — and its corollary, when it’s not, it isn’t.



*Shown in one of her many hats, Birnbaum told the audience, “We want you all to think big, be bold, and be active to help us identify the innovative elements that will provide guidance to the Institute over the next five years.” (Photo courtesy of Steve McCaw)*



## Order emerges from apparent chaos

For some, the Open Space method seemed like a prescription for chaos, but early in the series of six group break out sessions and discussions over refreshments and meals, it was clear that the process was working, as proposed topics began to address the larger issue of how a united NIEHS can move environmental health forward.

As one of their final activities on July 14, participants took the five stickers they were given for voting and selected from among 12 strategic plan goals, the ones they thought most important to include in the final Strategic Plan (see [Strategic Planning Stakeholder Community Workshop Report for summaries of reports and priority topics](#)).

## An inclusive and transparent step toward the Strategic Plan

As the votes were tabulated, participants gathered for the final time in their plenary circle. They passed a microphone around the circle and people who felt moved to comment were encouraged to express their sentiments. Several of the speakers thanked Birnbaum and NIEHS Deputy Director Rick Woychik, Ph.D., for the opportunity to participate. Others thanked NIEHS for a transparent and inclusive experience that gave people who had never met in person before an opportunity to discover common ground.

Birnbaum brought out her guitar and closed the event with a song she wrote about the workshop, sung to the tune of Joan Baez's 1969 Woodstock rendition of "Joe Hill." It was a fun ending to an intense and highly productive endeavor.

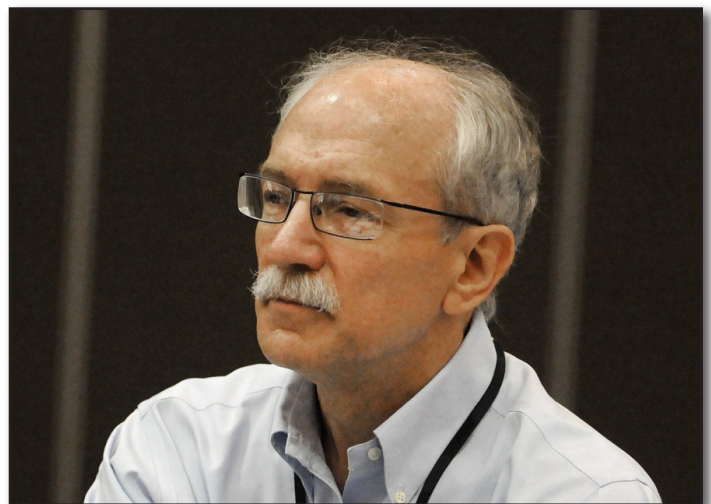
In October, a smaller group of stakeholders will meet to review all the workshop reports, along with all the ideas submitted through the website, to determine specific goals that will make up the new NIEHS strategic plan. Stay tuned for more updates and opportunities to provide comment.



*Williams worked the plenary circle as she explained the Open Space process and the rules that would govern the three days of discovery and consensus-seeking. (Photo courtesy of Steve McCaw)*



*Break out groups performed the nuts and bolts work of finding common ground and building a one-NIEHS perspective to integrate a wide range of agendas. (Photo courtesy of Steve McCaw)*



*Shown at one of the plenary circles, Woychik was both a participant and organizer of the workshop, as well as the lead in designing the yearlong series of activities that will culminate in mid-2012 with the new Strategic Plan. (Photo courtesy of Steve McCaw)*





*The process was difficult and sometimes messy, but as NIEHS Deputy Associate Director for Management Chris Long, above, discovered, also a time for laughter and banter. (Photo courtesy of Steve McCaw)*



*The Open Space process made for some unexpected, but productive, pairings of group fellows, such as NIEHS grantee and University of Rochester toxicologist Paige Lawrence, Ph.D., left, and NIEHS Acting Director of Clinical Research Darryl Zeldin, M.D., right. (Photo courtesy of Steve McCaw)*



*NIEHS epidemiologist Richard Kwok, Ph.D., cast one of his votes for strategic goals placed on the agenda wall. (Photo courtesy of Steve McCaw)*



*Birnbaum expressed her gratitude to participants with a folk song that moved the audience and closed the historic workshop. (Photo courtesy of Steve McCaw)*



*In a closing open mic comment that must have gratified organizers, NTP scientist Nigel Walker, Ph.D., center, said of the way the workshop led to discovery, "I found out something that I didn't know I was passionate about." (Photo courtesy of Steve McCaw)*

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# Interns enjoy program of career narratives

By Josh Zeldin

As part of the [NIEHS Summer Internship Program \(SIP\)](#), five panelists gathered June 23 to describe their career pathways and answer questions about their experiences in biomedical research. The panel discussion, titled “Career Opportunities in the Biomedical Sciences,” took place in the NIEHS Rodbell Auditorium and was organized by SIP coordinator Debbie Wilson.

Following a short introduction by Wilson, the panelists took turns informally discussing their professions in the field of biomedical science. From backgrounds as varied as growing up with parents who were physicians as career models, to breaking away from a blue-collar family’s expectations, the panelists recounted the various paths that led them ultimately to where they are today.

With candor and humor, the personal narratives helped an audience of young people, still unsure of their exact career directions, realize that others had shared their uncertainty and still managed, through persistence and, sometimes, sheer serendipity, to find success and satisfaction in their biomedical careers.

## Lessons from experience

Physician researcher [Stavros Garantziotis, M.D.](#), a principal investigator in the NIEHS Laboratory of Respiratory Biology (LRB) who is also involved in clinical research, was the first panelist to speak. Garantziotis stressed the background and experiences that led him into the field of medicine as a clinical and basic researcher, as well as the happenstance that brought him, finally, to NIEHS.

“Medicine is a vocation, not a 9-to-5 job,” said Garantziotis. You have to have an understanding spouse to be successful.”

Neuroscientist [Patricia Jensen, Ph.D.](#), a principal investigator in the NIEHS Laboratory of Neurobiology, spoke of her uncertainty regarding what field of science she wanted to pursue and her ten years in the workplace before she began her college education.

“I’ve always loved science,” said Jensen, “but you don’t ever really know what you want to do early on.” Nevertheless, she insisted, “It’s only going to get better, if this is what you truly love. Just make sure you love what you do.”



Host Debbie Wilson, center, chatted with panelists as interns began to fill Rodbell Auditorium. (Photo courtesy of John Maruca)



Seated, left to right, Garantziotis, left, who led off the discussion, Jensen, London, Malarkey, and Higgins, right. (Photo courtesy of John Maruca)



NIEHS epidemiologist [Stephanie London, M.D., Dr.PH.](#), and NTP veterinary pathologist [David Malarkey, D.V.M., Ph.D.](#), who followed Jensen, reinforced these messages concerning a career in the sciences, and talked frankly about the impact of the extra time and effort it took to complete their dual doctorates.

“You can [still] have a life and all that education,” Malarkey reassured the interns. “I got my first job at 37.”

### **Vocation motivated by love**

For her part, London, who also holds an appointment in LRB, expressed the importance of joy in selecting the type of career to pursue, of finding something, as she said, “That floats your boat.”

“If you aren’t really happy to get a paper accepted in a journal,” London pointed out, “then research is not for you. Whatever you’re doing, make sure the reward makes you happy.”

Science educator [William Higgins, Ph.D.](#), a University of Maryland professor of biology who also works with the NIH Office of Intramural Training and Education, emphasized initiative and the value of networking.

“If you’re assertive, confident, smart, etc., you can do whatever you want,” said Higgins, who has received a long list of awards for excellence in teaching, advising, and mentoring students over the course of his nearly 40 year career as a professor.

In contrast to the previous emphasis on education, Higgins argued that the key to success lay not only in what students do or how they get where they’re going, but also in the relationships they form along the way.

“I hang out with a bunch of intelligent people all day,” Higgins said of his experience as a student and later professor in academia. “I’ve never had a [real] job.” As he told the audience, love what you do and whom you do it with, and good fortune will come easily.

(Josh Zeldin is a summer intern with the NIEHS Office of Communications and Public Liaison. He is a student at the University of North Carolina at Chapel Hill.)



*Jensen recalled the sheer joy she felt when she was awarded a \$12,000 annual stipend in graduate school to do what she loves doing. The income, even at that near-poverty level, helped her gain the confidence to keep striving to realize her goals. (Photo courtesy of John Maruca)*



*For Higgins, the panel discussion was the beginning of a busy day at NIEHS. Later on, he presented talks directed toward students trying to get into graduate school and for ones aspiring to attend medical school. (Photo courtesy of John Maruca)*

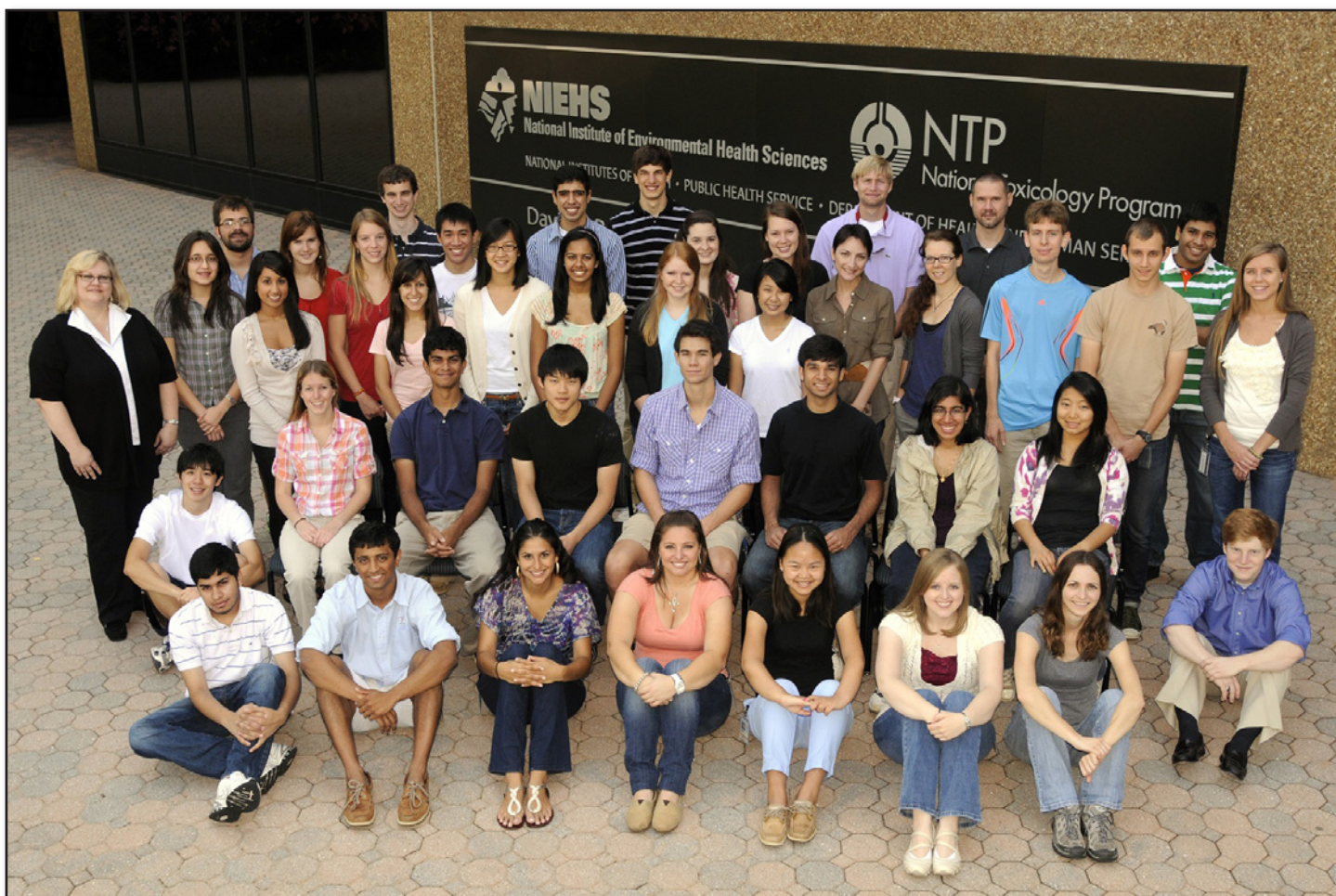




*As this show of hands suggests, the interns stayed engaged throughout the program and participated in the question-and-answer session that followed the panel presentations. (Photo courtesy of John Maruca)*



*Neurotoxicology Group summer intern Amanda McLean was one of several in the audience with questions for the panelists. (Photo courtesy of John Maruca)*



*The following week, the class of 2011 gathered in front of the main NIEHS building for the program's traditional group photo. (Photo courtesy of Steve McCaw)*



# Research fellow joins faculty at the University of South Carolina

By Archana Dhasarathy

Research Fellow [Minsub Shim, Ph.D.](#), left NIEHS this summer to assume an assistant professorship in the [Department of Biological Sciences](#) at the University of South Carolina. He spent the last eight years in the [Eicosanoid Biochemistry Group](#) of the [Laboratory of Molecular Carcinogenesis \(LMC\)](#) with NIEHS Principal Investigator [Thomas Eling, Ph.D.](#)

## A diverse scientific career

A native of South Korea, Shim started his scientific career working on purification and characterization of the DNA topoisomerase I enzyme in the laboratory of [Hyeon-Sook Koo, Ph.D.](#), in the Department of Biochemistry at Yonsei University in Seoul, Korea.

Shim came to the United States in 1998 to pursue his Ph.D. in the laboratory of [Robert Smart, Ph.D.](#), in the [Department of Environmental and Molecular Toxicology](#) at North Carolina State University (NCSSU). His research focused on the function and regulation of basic-leucine zipper (bZIP) transcription factors in keratinocyte growth and differentiation.

After he successfully defended his dissertation, Shim moved to the NIEHS to start work on the function and regulation of NSAIDs activated gene-1 (NAG-1) in prostate cancer. More recently, he initiated a project on cyclooxygenase-2 (COX-2) signaling in cancer and embryonic development.

Shim has authored many publications during his graduate and postdoctoral career. In 2008, he applied for and was awarded the prestigious NIH Pathway to Independence Award (K99/R00) from NIEHS.

## Networking and mentoring play important roles in career success

According to Shim, his helpful colleagues and co-workers at NIEHS played a key role in his success. “My time at NIEHS was the happiest in my life,” he said. “I was really fortunate to work with people who helped me along the way. I have learned that the most important thing in career success is not just hard work and luck, but to maintain a good relationship with the people around you,” he added.

Shim’s co-workers applauded both his perseverance and his willingness to help them. “Minsub is our lab’s go-to person for both technical questions and scientific discussion,” said [Justin Kosak](#), a biologist in the Eling laboratory. Kosak attributes Shim’s success to his passion for science. “He knows what he wants and is willing



*Shim will be starting his position this fall at the University of South Carolina's 206-year-old [campus](#) in Columbia. (Photo courtesy of Steve McCaw)*



*Eling said he was confident that Shim would be highly successful and he wished him only the best. (Photo courtesy of Steve McCaw)*



to work extremely hard to get it. Yet, he is also extremely humble and self-critical,” he added. [Xingya Wang, Ph.D.](#), a visiting fellow in the Eling laboratory, agreed. “Minsub is very warm hearted, and he is always willing to help even when he is very busy with his own experiments,” she said.

Shim acknowledged his mentor, Eling, for his help and encouragement during his postdoctoral tenure at NIEHS. Eling, in turn, had nothing but praise for his mentee. “I have been a mentor for many postdoctoral trainees over the years, and I think Minsub Shim is one the most dedicated and persistent scientists I have ever trained,” said Eling. “He is also one of the hardest working, with excellent molecular biology and critical thinking skills,” he added.

Shim also credited his mentor at NCSU, Smart, and Principal Investigator [Paul Wade, Ph.D.](#), head of the LMC Eukaryotic Transcriptional Regulation Group, for his career success. “Drs. Smart, Wade, and Eling helped me not only scientifically, and with my career development, but also emotionally through the rough stages in my career. I am highly indebted to them,” Shim said.

He also credits Microarray Group Technical Laboratory Manager Kevin Gerrish, Ph.D., and Julie Foley, group leader, [Special Techniques Group](#), for their unstinting help and advice. “They really encouraged me and helped me a lot, especially when I was discouraged by my experimental failures,” Shim added.

Shim’s colleagues at NIEHS wished him all the best in this important next step in his career.

(Archana Dhasarathy, Ph.D., is a postdoctoral fellow in the Eukaryotic Transcriptional Regulation Group in the NIEHS Laboratory of Molecular Carcinogenesis.)

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## Fellows fare well in 2012 award competition

*By Eddy Ball*

NIEHS excelled once again during the 2012 NIH Fellows Award for Research Excellence ([FARE](#)) competition, with NIEHS trainees receiving 21 of the prestigious awards.

Two NIEHS fellows were repeat winners — Xueqian (Shirley) Wang, Ph.D., with her third consecutive award, and Saurabh Chatterjee, Ph.D., with his second. Two groups had more than one member who received FARE awards this year — three fellows from the [Cell Biology Group](#) led by Chief of the Laboratory of Respiratory Biology Anton Jetten, Ph.D., and two from a Biostatistics Branch [Bioinformatics Group](#), led by Principal Investigator Raja Jothi, Ph.D.

NIEHS fellows received nearly 10 percent of the 218 awarded this year to fellows in training at the 27 NIH institutes and centers (ICs) by the NIH Fellows Committee (FelCom) FARE Subcommittee. Although NIEHS is in the midrange in terms of size and budget among the NIH institutes, the Institute placed among the top five in number of awards.

FARE awards are the result of peer review by special study sections of the abstracts submitted by fellows. The awards reflect the scientific excellence of the winners, the quality of the NIEHS training and career development program, and the superior mentoring that takes place in the Institute’s labs.

The FARE program is sponsored by the FelCom, Offices of the Scientific Directors, the NIH Office of Research on Women’s Health, and the NIH Office of Intramural Training and Education, and is funded by the Scientific Directors and the Office of Research on Women’s Health. Fellows submit abstracts based on their research, which are reviewed and ranked by panels of senior scientists.

The prizes are both an honor and a source of additional support for trainee professional and career development:

- A \$1000 travel award to attend a scientific meeting at which they present their work
- An invitation to present their posters at the annual Research Festival and attend the FARE award ceremony held in October
- Eligibility to serve as judges for the following year's FARE competition

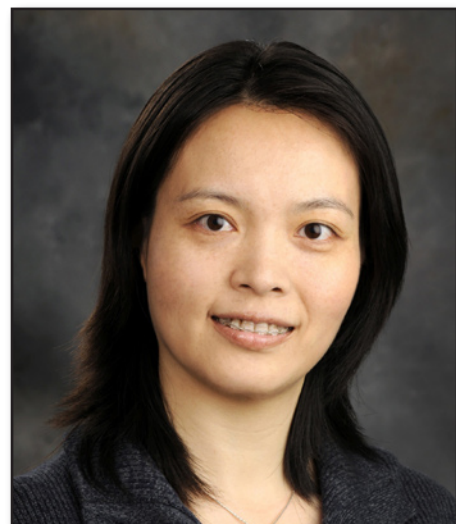
Photo credits include trainee's name, abstract title, and mentor. Abstracts are posted [online](#).



*Intramural Research and Training (IRTA) Fellow [Joseph Burgents, Ph.D.](#), "CD103+ and CD11b+ pulmonary dendritic cells display distinct migratory properties during steady-state and following allergic sensitization," Principal Investigator [Donald Cook, Ph.D.](#) (Photo courtesy of Steve McCaw)*



*IRTA Fellow [Nisha Cavanaugh, Ph.D.](#), "New Insights into Ribonucleotide Discrimination by DNA Polymerase Beta," Principal Investigator [Samuel Wilson, M.D.](#) (Photo courtesy of Steve McCaw)*



*Visiting Fellow [Xiaoqing Chang, Ph.D.](#), "A Physiologically Based Pharmacokinetic Model of Micro and Nano Sized Fluorescent Polystyrene Spheres in Rats," NTP Biomolecular Screening Branch Chief [Ray Tice, Ph.D.](#) (Photo courtesy of Steve McCaw)*



*Visiting Fellow [Saurabh Chatterjee, Ph.D.](#), "Leptin signaling synergizes environmental bromodichloromethane exposure-induced post translational protein oxidations, antigen presentation and exacerbation of steatohepatitis of obesity," Principal Investigator [Ronald Mason, Ph.D.](#) (Photo courtesy of Steve McCaw)*



*Research Fellow [Saiful Chowdhury, Ph.D.](#), "Proteomic analysis of lipid rafts from ATP Binding Cassette Transporter A1-deficient macrophages reveals novel regulatory events in the innate immune response," Principal Investigator [Michael Fessler, M.D.](#) (Photo courtesy of Steve McCaw)*



*Research Fellow [Johannes M. Freudenberg, Ph.D.](#), "A meta-analysis reveals novel regulators required for mouse embryonic stem cell self-renewal," Principal Investigator [Raja Jothi, Ph.D.](#) (Photo courtesy of Steve McCaw)*

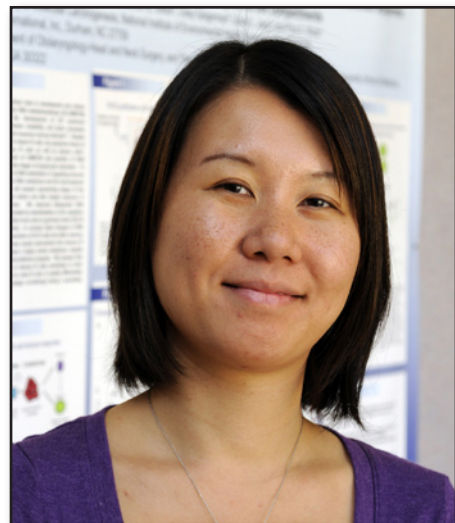




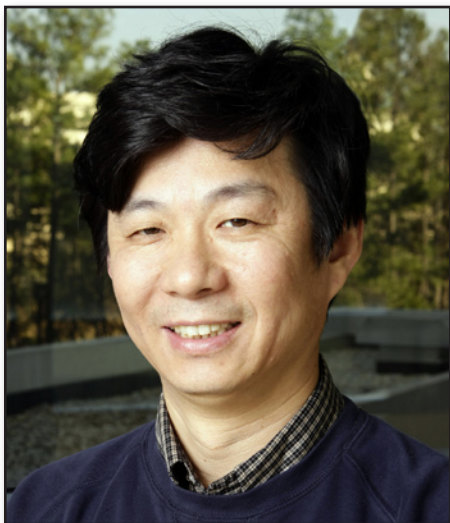
Research Fellow [Huiming Gao, M.D., Ph.D.](#), “HMGB1 (high-mobility group box 1) acts on microglia Mac1 (macrophage antigen complex 1) to mediate chronic neuroinflammation that drives progressive neurodegeneration,” Principal Investigator [Jau-Shyong Hong, Ph.D.](#) (Photo courtesy of Steve McCaw)



IRTA Fellow [Jill Hesse, Ph.D.](#), “Identification and Discovery of DNA Damage-Induced microRNA Expression Changes by Microarray and Next-Generation Sequencing in Wild-Type and ATM-Deficient Human Mammary Epithelial Cells,” Principal Investigator [Richard Paules, Ph.D.](#) (Photo courtesy of Steve McCaw)



IRTA Fellow [Anne Lai, Ph.D.](#), “DNA methylation primes the memory B cell epigenome for plasma cell differentiation,” Principal Investigator [Paul Wade, Ph.D.](#) (Photo courtesy of Steve McCaw)



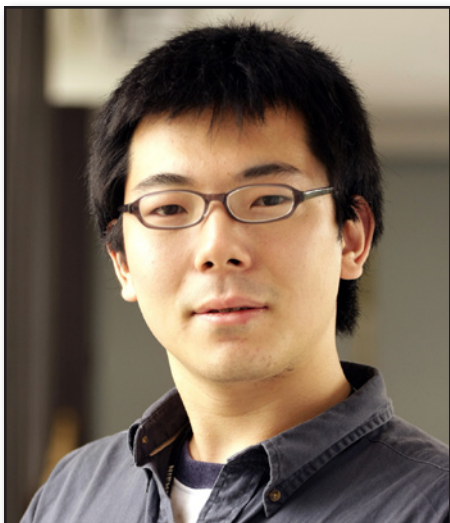
Research Fellow [Hong Li, M.D.](#), “Cyclooxygenase-2 (COX-2) Negatively Regulates IL-9+/CD4+ T cells (Th9) Differentiation during Allergic Lung Inflammation through down-regulation of IL-17RB,” Principal Investigator [Darryl Zeldin, M.D.](#) (Photo courtesy of Steve McCaw)



IRTA Fellow [Kristin Lichti-Kaiser, Ph.D.](#), “The Role of Glis3 in the Development of Functional Pancreatic Beta-cells and Diabetes,” Principal Investigator [Anton Jetten, Ph.D.](#) (Photo courtesy of Steve McCaw)



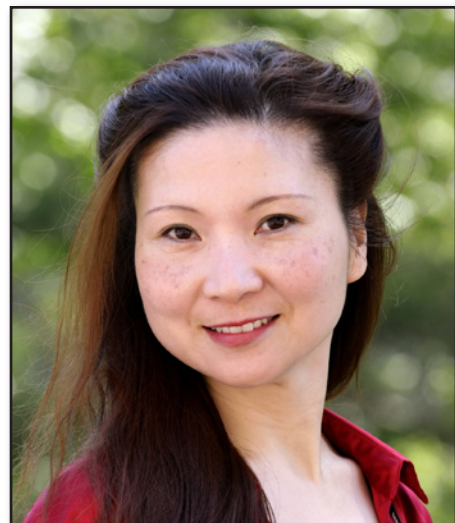
Special Volunteer [Leelavati Narlikar, Ph.D.](#), “Genome-wide characterization of CTCF’s role as an enhancer-blocker,” Principal Investigator [Raja Jothi, Ph.D.](#) (Photo courtesy of Leelavati Narlikar)



Visiting Fellow [Kosuke Saito, Ph.D.](#),  
“The role of the potassium channel  
KCNK1 in the sexual dimorphic  
centrilobular hypertrophy induced by  
phenobarbital in mouse liver,” Principal  
Investigator [Masahiko Negishi, Ph.D.](#)  
(Photo courtesy of Steve McCaw)



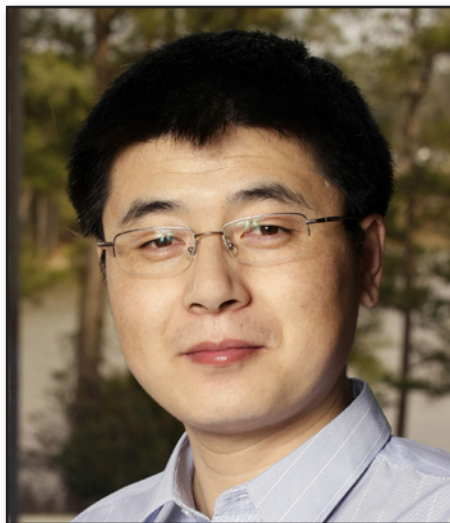
Visiting Fellow [Yukimasa Takeda, Ph.D.](#),  
“Retinoic acid-related orphan receptor  
gamma, RORgamma, coordinates  
the circadian regulation of energy  
homeostasis through the control of  
hepatic lipid and glucose metabolism,”  
Principal Investigator [Anton Jetten,  
Ph.D.](#) (Photo courtesy of Steve McCaw)



IRTA Fellow [Percy Tumbale, Ph.D.](#),  
“Structural Basis of DNA Ligase  
Proofreading by Aprataxin with insights  
into AOA1 Neurodegenerative Disease,”  
Principal Investigator [Scott Williams,  
Ph.D.](#) (Photo courtesy of Steve McCaw)



IRTA Fellow [Kirsten Verhein, Ph.D.](#),  
“Candidate susceptibility genes  
in a murine model of RSV-induced  
bronchiolitis,” Principal Investigator  
[Steven Kleeberger, Ph.D.](#) (Photo  
courtesy of Steve McCaw)



IRTA Fellow [Huanchen Wang, Ph.D.](#),  
“Substrate Specificity and Catalysis  
Mechanism of Inositol Pyrophosphate  
Kinase,” Principal Investigator  
[Stephen Shears, Ph.D.](#) (Photo courtesy  
of Steve McCaw)



Research Fellow [Xueqian \(Shirley\)  
Wang, Ph.D.](#), “Nuclear Factor E2-  
Related Factor-2 (Nrf2) Regulates  
P-glycoprotein Expression at the  
Blood-Brain Barrier (BBB) by Acting  
Through p38 MAP Kinase,” Principal  
Investigator [David Miller, Ph.D.](#) (Photo  
courtesy of Steve McCaw)





Research Fellow [Wipawee \(Joy\) Winuthayanon, Ph.D.](#), “Role of epithelial estrogen receptor alpha in the oviduct during fertilization and embryo development,” Principal Investigator [Kenneth Korach, Ph.D.](#) (Photo courtesy of Steve McCaw)



Research Fellow [Mengyuan \(Tracy\) Xu, Ph.D.](#), “coMOTIF: A Mixture Framework for Identifying Transcription Factor and a Co-regulator Motifs in ChIP-seq Data,” Principal Investigator [Leping Li, Ph.D.](#) (Photo courtesy of Jennifer Weinberg)



Visiting Fellow [Zhengyu Yin, Ph.D.](#), “RAP80 Plays a Critical Role in Maintaining Genomic Stability and Tumor Suppressing,” Principal Investigator [Anton Jetten, Ph.D.](#) (Photo courtesy of Steve McCaw)

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## NTP fellow wins travel award

*By Eddy Ball*

NTP [Toxicology Branch](#) Research Fellow [Mamta Behl, Ph.D.](#), received a \$1000 travel award from the Society of Toxicologic Pathology to attend the [annual meeting](#) held June 19-23 in Denver.

Behl presented a poster on NTP research on “Peripheral Neuropathy in Rats Exposed to Styrene Acrylonitrile (SAN) Trimer.” SAN Trimer is a by-product of the production of acrylonitrile styrene plastics and is created in specific manufacturing processes for polymers of acrylonitrile and styrene. NTP conducted two-year chronic feeding studies exposing rats to SAN Trimer in a perinatal-postnatal exposure design. Findings from the NTP studies on SAN Trimer were peer-reviewed at a public meeting Jan. 26 ([see story](#) and [NTP peer review](#)).

Other members of the research team included lead NTP toxicologist [Rajendra Chhabra, Ph.D.](#); NIEHS biostatistician [Grace Kissling, Ph.D.](#); lead NTP pathologist [Susan Elmore, D.V.M.](#); former NTP Research Fellow [Deepa Rao, BVSc, Ph.D.](#), now of Integrated Laboratory Systems, Inc.; James Morrison, D.V.M. of Charles River Laboratories, Pathology Associates; and Amy Brix, D.V.M., Ph.D., of Experimental Pathology Laboratories. Chhabra is Behl’s current mentor.



*Behl received a travel award to attend Society of Toxicology Pathology annual meeting in June. (Photo courtesy of Steve McCaw)*

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# NTP postdocs pass laboratory animal medicine boards

*By Eddy Ball*

NTP postdoctoral fellows Jacquelyn (Jai) Tubbs, D.V.M., and Coralie Zegre-Cannon, D.V.M., learned in July that they've taken an important step in their careers by satisfying requirements for certification as Diplomates of the [American College of Laboratory Animal Medicine \(ACLAM\)](#). Tubbs is currently a member of the [NTP Laboratory Animal Management Group](#) headed by Angela King-Herbert, D.V.M., who oversees the fellowship in Laboratory Animal Medicine training program within the NTP Cellular and Molecular Pathology Branch (CMPB). Zegre-Cannon was also part of the group until December 2010.

In a message to the new diplomates, Molecular Pathology Group Leader and CMPB Chief [Robert Sills, D.V.M., Ph.D.](#), congratulated Tubbs and Zegre-Cannon. "This is a major achievement and a significant success for yourself and the NTP Training Program."

Sills also praised King-Herbert for her leadership. "This is also a tremendous honor for yourself as the head of the training program and to all your lab animal medicine colleagues at NIEHS and in the RTP [Research Triangle Park, N.C.] who partnered with you in making the training program a success," he wrote. "Having 100 percent success for the first trainees in the NTP Laboratory Animal Medicine Training Program is outstanding."

## ACLAM Diplomates

ACLAM Diplomates are involved in a wide variety of activities, including management and direction of animal resource facilities and programs; clinical medicine, surgery, and programs of disease prevention; consultation on the care and use of laboratory animals; assisting institutions in achieving compliance with animal care and use regulations; collaborative and independent research; and instruction and training, including informing the public about the humane use of animals in biomedical research.

ACLAM recertification is required at eight-year intervals, commencing with the first calendar year following initial certification. The recertification periods are staggered so that only about one-eighth of the ACLAM membership comes up for recertification each year. A total of 400 recertification credits must be attained during each recertification period.

## NTP training in laboratory animal medicine

As part of the NTP Laboratory Animal Management Group, Tubbs and Zegre-Cannon are part of the oversight effort for the laboratory animal-related matters for the NTP, including:



*Jacquelyn Tubbs, D.V.M., DACLAM (Photo courtesy of Steve McCaw)*



*Coralie Zegre-Cannon, D.V.M., DACLAM (Photo courtesy of Steve McCaw)*



- Assisting in the selection and provision of disease-free genetically defined rodent models, as well as monitoring animal care and use in NTP studies.
- Aiding in the preparation of NTP Technical Reports.
- Advising the NTP on animal care and animal welfare issues.

The fellowship in Laboratory Animal Medicine is designed for individuals to participate in NTP and NIEHS laboratory animal veterinary care. The training program includes clinical and surgical responsibilities, animal care facility management, participation in research projects, and laboratory animal pathology. In addition to trainees being involved in a variety of laboratory animal science settings, they also have the opportunity to attend outside training activities and scientific meetings, as well as to engage in collaborative research with NTP and NIEHS scientists. Trainees also have clinical responsibilities and participate in training at the nearby University of North Carolina at Chapel Hill Division of Laboratory Animal Medicine.

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## Henry and Thigpen Tart accepted in leadership program

*By Eddy Ball*

Two NIEHS employees, Heather Henry, Ph.D., and Kimberly Thigpen Tart, J.D., will be a part of the inaugural [NIH Mid-Level Leadership Program](#) in fiscal year 2012.

Henry is currently a health scientist administrator in the [NIEHS Superfund Research Program](#). Thigpen Tart is a program analyst in the [NIEHS Office of Policy, Planning, and Evaluation](#).

### An exciting new opportunity

Acceptance into the program's single class of 28 employees in its initial year was especially competitive, explained NIEHS Deputy Associate Director for Management Chris Long. "In future years, OHR [the NIH Office of Human Resources] expects to provide expanded opportunities [with] potentially multiple classes, which would give a great opportunity for more people to participate," he said.

The NIH Mid-Level Leadership Program provides GS-12/13/14 and equivalent employees with the leadership skills and knowledge to aid them in effectively leading from both supervisory and non-supervisory positions. Unlike U.S. Office of Personnel Management-mandated supervisory training programs targeting technical supervisory skills, the Mid-Level Leadership Program emphasizes the leadership developmental areas of self-awareness and fulfilling the leadership function, understanding and collaborating with others, and strategic business acumen.



*Henry oversees several major NIEHS Superfund grants. (Photo courtesy of Steve McCaw)*

Henry and Thigpen Tart will join their fellow participants in Bethesda, Md., for five two-day training sessions taking place over a period of six months, as well as mentoring and support activities. As part of their experience, between sessions, participants will have on-the-job assignments, where they can apply what they have learned in the workplace.

The Mid-Level Leadership Program is one of several programs offered by the [NIH Training Center](#), which is the dedicated resource for NIH-specific training, professional development programs, and customized solutions to ensure that institutes and centers have a steady supply of talent to provide quality leadership now and into the future.

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*Thigpen Tart was part of the editorial team responsible for the 2010 white paper, “[A Human Health Perspective on Climate Change](#).” (Photo courtesy of Steve McCaw)*

## Former NIEHS trainee to spearhead expansion of cancer registry

*By Ian Thomas*

An alumna of the [NIH Graduate Partnerships Program](#) and a highly successful breast cancer researcher at the University of Miami, Tonia Hermon, Ph.D., prepares to return home to St. Thomas in the U.S. Virgin Islands where she’ll begin a new phase in her professional life. There, she hopes to give back to her native community by exploring the environmental influences on area public health, as she sets up the territorial government’s first-ever comprehensive cancer registrar.

“In a lot of ways, the waters back home are the lifeblood of the local economy and while they’ve conducted an extensive amount of marine research over the years, there’s been little attention paid to the environmental impact on the area’s cancer rate,” Hermon points out. Still, she freely admits that the joy over her homecoming is far from professionally exclusive. “It’s going to be a big change, but I’m really excited. I still have family down there and it’s been a long time since I’ve lived back home.”

### In training at NIEHS

A graduate of the Eastern Virginia Medical School and Old Dominion University’s joint doctoral program in biomedical sciences, Hermon quickly established herself as one of NIEHS’ promising trainees when her first ever poster presentation on uterine fibroids, titled “Phospho-Serine-118 Estrogen Receptor Alpha (ERalpha) is Highly Expressed in Human Uterine Leiomyoma Compared to Myometrial Tissue,” was awarded an Honorable Mention at the 2006 Global Challenges, Local Solutions Research Expo in Norfolk, Virginia.



*Hermon hopes to one day launch a cancer research laboratory in her native U.S. Virgin Islands. (Photo courtesy of Steve McCaw)*



“Tonia is a total success story, not only for my lab, but for the entire NIEHS family,” said [Darlene Dixon, D.V.M., Ph.D.](#), head of the NTP Comparative Pathobiology Group and Hermon’s mentor.

“We’ve trained an individual who went on to become a highly successful researcher at a fast-paced university like Miami and now she’s going back to make a difference in the community that she grew up in. We should all be proud of her.”

### Focusing on reproductive disease and cancer

In addition to geographical diversity, Hermon’s career has also been defined by her breadth of research into various forms of reproductive disorders and cancer. Following her time at the Institute from 2004 to 2009, where she focused primarily on uterine leiomyomas, Hermon accepted a postdoctoral fellowship to study breast cancer with the [University of Miami Sylvester Comprehensive Cancer Center](#), though her interest in the disease began long before her entrance into academia.



*Dixon, left, joins Hermon at the bank of microscopes where they have spent so many hours working side by side. Dixon said that working with a doctoral student required more direct supervision than she’d realized at first, but the outcome was well worth the extra effort. (Photo courtesy of Steve McCaw)*

“Coming out of college, I was extremely committed to working in the reproductive field,” she recalls. “When I was young, both my mom and my aunt were diagnosed with uterine leiomyomas. So from a research standpoint, that really served to keep me focused. Plus, this is something that affects a lot of African-American women during their reproductive years and being a mom myself, it’s an issue that really hits home for me.”

## Improving public health and promoting prevention

Hermon has a number of questions she hopes to answer through the expanded registry. “They just don’t have the information base there that we have here on the mainland,” she explained. “What forms of cancer are prevalent in the local population? If they’re getting breast cancer, what kind of breast cancer? What sort of treatments and medications are they receiving? Which are working? Which are not and why? What are the causes? Could they be environmental? These are the questions that need answers and the establishment of a comprehensive cancer registry will go a long way toward helping to solve them.”

In the end, her mentor and others agree, Hermon is the right person to tackle the challenge.

“She’s simply perfect for this job,” Dixon exclaims. “She was raised there, went to high school there, and then left the island to go receive her education on the mainland. Now she’s coming back in the type of position that will not only advance the area’s knowledge of cancer and its treatment avenues, but also help to foster a better relationship between her community and the local government. She’s perfect, simply perfect.”

(Ian Thomas is a writer/editor in the NIEHS Office of Communication and Public Liaison)

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# Mutation cluster discovery wins postdoc Roberts a poster prize

By Eddy Ball

NIEHS postdoctoral fellow [Steven Roberts, Ph.D.](#), added yet another award to his list of honors with a best poster win at the 2011 Gordon Research Conference (GRC) on Genetic Toxicology. Roberts presented research he conducted with members of the NIEHS Laboratory of Molecular Genetics (LMG) Chromosome Stability Group and colleagues at the University of North Carolina at Chapel Hill (UNC-CH), titled “Damage-Induced Localized Hypermutability at Double-Strand Breaks and Replication Forks.”

In her message of congratulations, Cell Press Marketing/Publicity Coordinator Mary Beth O’Leary told Roberts he would receive a complimentary subscription to the journal *Molecular Cell*, sponsor of the poster competition. Cell Press also congratulated Roberts July 24 on its Facebook page and at CellPressNews on [Twitter](#).

Held July 10-15 in Barga, Italy, the conference also featured oral presentations by one of Roberts’ mentors, Principal Investigator [Michael Resnick, Ph.D.](#); Laboratory of Structural Biology (LSB) Chief and LMG Principal Investigator [Thomas Kunkel, Ph.D.](#); and LSB DNA Repair and Nucleic Acid Enzymology Group Principal Investigator Samuel Wilson, M.D. Joining them as presenters was former LMG Principal Investigator Ben Van Houten, Ph.D., who is now at the University of Pittsburgh, and other leading authorities in genetic toxicology.



*Roberts also received a number of honors during his undergraduate years at Bowling Green State University, and in his graduate program in biochemistry and biophysics at UNC-CH. He has received several scholarships and, in 2003, was inducted into the Phi Beta Kappa Honor Society. (Photo courtesy of Steve McCaw)*

## Surprising discovery of large mutation clusters

According to Roberts, his team’s poster depicted work showing that chronic exposure of mitotic yeast to low levels of a DNA damaging agent results in the formation of large mutation clusters. Since mutations are traditionally perceived as random independent events, the investigators said they were surprised to discover these large mutation clusters, which contain as many as 30 simultaneous mutations and stretch across some 250 kilobases.

The team found that these clusters are targeted to areas of persistent single-strand (ss) DNA associated with DNA double-strand break repair and replication fork dysfunction. These ssDNAs accumulate DNA lesions that cannot be repaired and are subsequently converted to mutations by error-prone translesion synthesis.

“This is an important advance in the field as the simultaneous generation of mutations amplifies the number of tracks by which genetic changes may accumulate during evolution and in the onset of genetic disease,” Roberts explained. “Our work is the first to link the generation of mutation clusters to specific cellular processes like homologous recombination and replication.”

## Shaping a career while training at NIEHS

Roberts joined NIEHS as an Intramural Research Training Award fellow following completion of his doctorate at UNC-CH in 2008. Since then he has co-authored two publications, participated in five poster competitions, and delivered two invited talks at conferences. He has served as an NIEHS Summer Internship Program



mentor and an Undergraduate Research Program mentor. Roberts is a former LMG Trainee Action Committee representative and served as host for an LMG Fellows Invited Lecture Series presentation May 2 by cancer biologist Roger Greenberg, M.D., Ph.D. ([see story](#))

In addition to his win at GRC, Roberts was also recognized for the Best Oral Presentation at the fall 2010 meeting of the Genetics and Environmental Mutagenesis Society, winning a \$1,500 travel award ([see story](#)).

*Citation:* Roberts SA,\* Sterling J,\* Yang Y,\* Thompson C,\* Malc E,# Mieczkowski P,# Resnick MA,\* Gordenin DA.\* 2011. Damage-Induced Localized Hypermutability at Double-Strand Breaks and Replication Forks.

\* Chromosome Stability Group, Laboratory of Molecular Genetics, National Institute of Environmental Health Sciences, NIH, DHHS, Research Triangle Park, NC27709

# Department of Genetics, Carolina Center for Genome Sciences, University of North Carolina at Chapel Hill, NC 27599-3280

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## Neurobiologist McPherson wins travel award to meeting in Athens

*By Eddy Ball*

The first time NIEHS [Neurotoxicology Group](#) Technician Chris McPherson won a travel award to present his research at the annual meeting of the International Society for Neurochemistry (ISN), nature had other things in store. A category five hurricane lashed the coast of Cancun, Mexico, where the meeting was to be held, cancelling travel.

This summer, however, McPherson is confident he will fly to Athens, Greece for the [23rd biennial meeting](#) of [ISN](#) and the European Society for Neurochemistry Aug. 28-Sept. 1. McPherson is taking advantage of a prestigious, highly competitive [travel award](#) to present his research, “Potential contribution of resident microglia during injury-induced neurogenesis” ([see text box](#)) at the meeting.

McPherson is first author on the study with a prior NIEHS postdoctoral fellow, Andrew Kraft, Ph.D., as co-author, and [Jean Harry, Ph.D.](#), as lead author. Harry is NIEHS Neurotoxicology Group principal investigator, McPherson’s supervisor, and his advisor in the [Curriculum in Toxicology](#) at the University of North Carolina at Chapel Hill, where Harry holds an appointment as an adjunct faculty member.

### Finding career direction at NIEHS

McPherson came to NIEHS as a summer intern in 1999 with Harry’s group. At the time he was completing his undergraduate work in cell biology at Arizona State University and wondering what he wanted to do with his future. He returned after graduation in 2000 as an Intramural Research Training Award postbaccalaureate fellow in the group, as he said, “To make sure it’s really what I wanted to do.”



*Over the past decade as McPherson has worked in the lab and pursued his doctorate, he has also co-authored ten studies published by Harry’s group, including one the journal *Brain, Behavior, and Immunity* ([see story](#)) will highlight in a press release. (Photo courtesy of Steve McCaw)*

When McPherson finished his year as a postbac, instead of going to graduate school right away, he stayed on with Harry as a lab technician. By 2005, however, he'd decided to enter the Curriculum in Toxicology program with Harry as his advisor on the thesis he plans to defend in the fall. If everything goes as anticipated, McPherson will graduate with his Ph.D. in toxicology this December.

During his time with the group, McPherson has been Harry's protégée and advisee, as well as a mentor for summer interns in the lab. Among the bright young students McPherson has helped over the years is former Cary Academy student Anirudh Kota, who presented research he conducted with McPherson and Harry at the 2007 Society of Toxicology Annual Meeting and ToxExpo ([see story](#)). This summer, Harry and McPherson are working with summer intern Amanda McLean, a student at Oakland University, and Shreya Das, a high school student at Chapel Hill High.

### Deciding on the next big step

McPherson plans to continue working in the Neurotoxicology Group for the time being, at least until he has time to weigh his options for further career development. Harry's group is one of several that will become part of the new Division of NTP laboratory to be headed by NTP Principal Investigator Mike Waalkes, Ph.D., a development that McPherson thinks may open new opportunities for integrative research targeted toward human health.

"I'm interested in learning more about NTP and how its research on the potential toxicity of environmental agents helps shape regulatory decisions by such agencies as the [U.S.] Food and Drug Administration and the [U.S.] Environmental Protection Agency," he said. "I have received offers for post-doctoral fellowships, but I plan to weigh several options before I finally make a decision about my next step."

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## New findings about the brain's self repair after injury

McPherson's presentation is based on research he and his co-authors published in the February 2011 issue of [Neurotoxicity Research](#). His abstract for the meeting, below, offers an expanded context for their findings:

Adult neurogenesis occurs in the subgranular zone (SGZ) of the hippocampal dentate gyrus, generating new dentate granule neurons. This process can be induced with brain injury, suggesting a capacity for self-repair in the hippocampus. Both resident microglial cells and infiltrating macrophages produce inflammatory molecules in response to brain injury.

While inflammation has been reported to be detrimental to hippocampal neurogenesis, other studies have suggested, rather, that the localized inflammatory response and stimulation of microglial cells can promote neurogenesis. Thus the question arises, what distinguishes beneficial versus adverse effects of inflammation on neurogenic self-repair? It is our group's working hypothesis that activated resident microglia may serve a supportive role during injury-induced neurogenesis in the hippocampus.

To examine our hypothesis, we used the hippocampal toxicant, trimethyltin (TMT; 2.3 milligrams per milliliter, ip), as a tool to selectively target dentate granule cell death in adolescent CD-1 male mice. Within 48 hours post-TMT, neuronal death is accompanied by resident microglia activation, and elevations in tumor necrosis factor alpha (TNF $\alpha$ ) and interleukin-1 $\alpha$  (IL-1 $\alpha$ ) mRNA levels. Bromodeoxyuridine (BrdU) incorporation identified the peak time of neurogenesis as coinciding with peak of neuroinflammation.

BrdU+ cells were transiently in contact with process-bearing microglia within the SGZ and inner granule cell layer (GCL). The proliferative response was sufficient to fully repopulate neurons in the GCL and provide functional recovery. Using laser-capture microdissection, SGZs were isolated at 48 hours post-TMT for qPCR analysis. Key molecules in the interleukin-1 $\alpha$  pathway were induced by TMT exposure. Effects of IL-1 $\alpha$  [150 picograms per milliliter] were identified in the proliferation and differentiation of hippocampal neural progenitor cells (NPCs) *in vitro*.

These data suggest a role for resident microglia and secreted IL-1 $\alpha$  in regulation of NPC proliferation and differentiation for self-repair following chemical-induced hippocampal injury.



# Jung honored with mentoring award

*By Ian Thomas*

In recognition of his exemplary work within the Asian Pacific American medical community, NIEHS Chief of Staff Cmdr. Paul Jung, M.D., was honored on June 22 with the U.S. Public Health Service (USPHS) Asian Pacific American Officers' Committee RADM Samuel Lin Senior Officer Award at the 2011 Minority Officer Liaison Council (MOLC) awards ceremony in New Orleans. Held annually by the MOLC, the ceremony recognizes excellence on the part of individuals who continually strive to further the USPHS mission to protect, promote, and advance the health and safety of our nation.

“Reducing health disparities has been a long-standing priority for the [U.S.] Department of Health and Human Services [HHS],” Jung said. “I’m glad the committee has the opportunity to recognize officers who make the effort to contribute to the public’s health in this way.”

Prior to his arrival at NIEHS in February 2010 ([see related story](#)), Jung’s previous assignments included details to the House Energy and Commerce Committee and Peace Corps. As a graduate of the University of Maryland School of Medicine, he completed residencies in internal medicine at Case Western Reserve University and preventive medicine at Emory University. He earned his M.P.H. as a Robert Wood Johnson Clinical Scholar at Johns Hopkins University.

(Ian Thomas is a writer/editor for the NIEHS Office of Communications and Public Liaison)

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*Jung, left, is joined by are Rear Adm. Epifanio (Epi) Elizondo, Ph.D., HHS Region VI regional health administrator, center, and Capt. Lydia Soto-Torres, M.D., medical officer at the National Institute of Allergy and Infectious Diseases (right) during the award presentation. (Photo courtesy of Cmdr. David Lau)*

# Science Notebook

## NIEHS celebrates five years of ONES research

By Ernie Hood

NIEHS began the Outstanding New Environmental Scientist (ONES) Awards program in 2006, so this year the original class of grantees is now in the final year of their five-year ONES funding. With that in mind, at this year's ONES grantees forum held at NIEHS July 18-19, for the first time, all 35 current ONES researchers were invited to gather and share their science with each other and with their colleagues at NIEHS ([see text box](#)).

### Passing the Torch

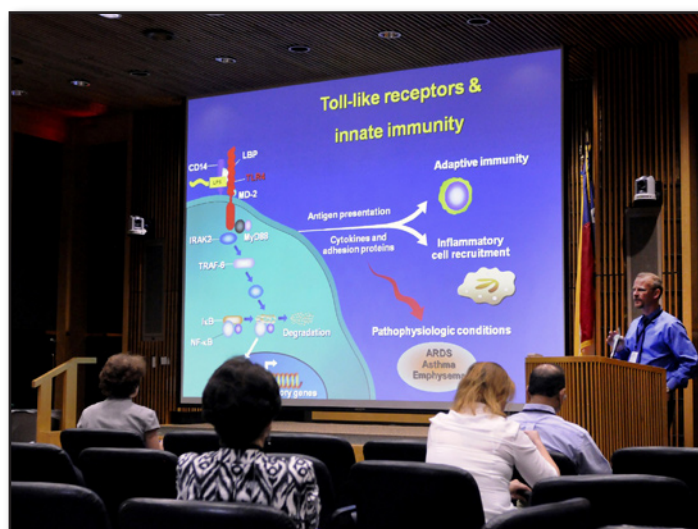
NIEHS Training and Career Programs Health Science Administrator Carol Shreffler, Ph.D., said there were two reasons for the decision to expand the annual forum to two days and include all of the existing grantees. "Since this was the year that the first class was in the fifth year of their award and they're transitioning off to other sources of funding, we wanted to have a combined meeting, so the younger people could learn from the older people, and so we could get an idea of what the spectrum of the program looked like," said Shreffler.

ONES was designed to attract young investigators into the field, to support their transition to independence, and to encourage a long-term commitment to environmental health science research by providing five years of substantial funding, protected time, and an advisory committee of senior experts in the field for scientific and career path advice.

NIEHS/NTP Director Linda Birnbaum, Ph.D., warmly welcomed the ONES scientists and praised their accomplishments. "There are so many things we're proud of regarding this program," she said. "For example, the diversity of the portfolio shows the connection between our health and the environment, with awardees spanning the breadth of the research NIEHS supports, from very basic molecular studies to clinical research and population-based studies. The complexity of the issues you're tackling shows the complicated landscape that is environmental health sciences."



*Calling it "one of my favorite meetings," Birnbaum welcomed the five classes of ONES awardees to the two-day forum, where they had the opportunity to present their research to each other and interested NIEHS personnel. (Photo courtesy of Steve McCaw)*



*2008 ONES awardee John Hollingsworth, M.D., of Duke University Medical Center, briefed attendees on his work, which has shown that ozone primes pulmonary innate immunity. (Photo courtesy of Steve McCaw)*



## ONES, enabling early career milestones

As they made their [scientific presentations](#), each of the ONES awardees in attendance spoke glowingly about the program, sincerely grateful for the support that had so changed their lives and the lives of many of their colleagues. “It’s definitely letting us do some wildly crazy, exciting, and what we hope will eventually be beneficial work here,” said Joseph Shaw, Ph.D., of Indiana University, a 2010 ONES grantee who is researching the effects of environmental contamination on gene copy number variation.

Thomas Begley, Ph.D., of the University at Albany - State University of New York, one of the original 2006 class of ONES awardees, said, “The program has allowed me to launch my program and to develop research expertise and resources that allowed me to take basic research findings into human health and exposure biology.” West Virginia University researcher and 2007 ONES recipient Timothy Nurkiewicz, Ph.D., said, “It literally created my career, and it has spawned four other investigators in this field from my lab. Also, it’s created a second laboratory in my institution, an inhalation facility specific for environmental sciences,” he added.

Stephania Cormier, Ph.D., of Louisiana State University has already contributed significantly to the field with her work on combustion-generated PM<sub>0.1</sub> and predisposition to asthma. She said that rather than simply funding an individual project, ONES helped her develop “a program where I can look at and understand a variety of exposures and how they lead to long-term airway disease. It allowed me to get equipment in my lab that most R01s [research project grants] don’t, and to set up a mentoring team that could help guide me through my first R01 and deal with the administrative side of the grant. It also put me in contact with people here at NIEHS who’ve allowed me to develop grants and projects as offshoots of the original project.”

Although the ONES funding announcement will not continue past the 2011 class of grantees, which will be announced shortly, all current awards will last the full five years and, in the future, NIEHS will employ other mechanisms to continue to identify and fund outstanding early-stage investigators in environmental health sciences.

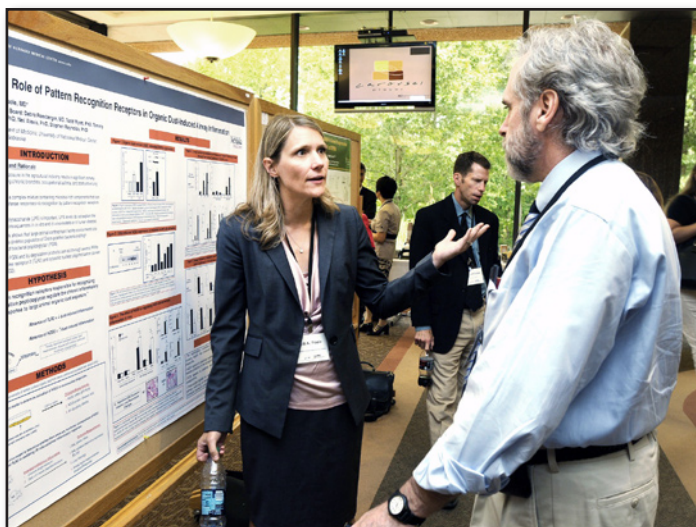
(Ernie Hood is a contract writer with the NIEHS Office of Communications and Public Liaison.)



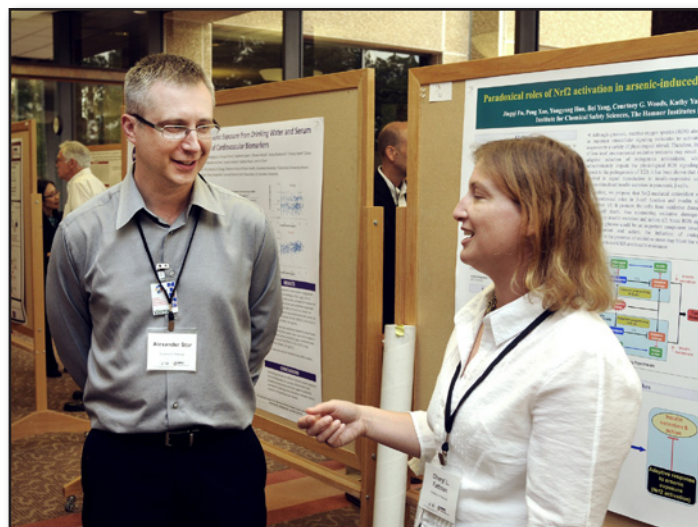
*ONES program director Shreffler was gratified by the high quality of the science presented at the grantees forum. (Photo courtesy of Steve McCaw)*



*Jill Poole, M.D., of the University of Nebraska Medical Center, shared her research on the role of pattern recognition receptors in organic dust-induced airway inflammation. (Photo courtesy of Steve McCaw)*



Each of the ONES awardees also presented a poster in the lobby outside the meeting room. Poole, left, discussed hers with DERT Deputy Director Pat Mastin, Ph.D. (Photo courtesy of Steve McCaw)



ONES awardees Alexander Star, Ph.D. (2010), and Cheryl Fattman, Ph.D. (2007), both of the University of Pittsburgh, compare notes at the meeting's poster session. (Photo courtesy of Steve McCaw)

## A division-wide affair

The ONES grants spanned a number of portfolios within the NIEHS Division of Extramural Research and Training (DERT). Consequently, when Shreffler organized this lineup of top young investigators funded by NIEHS, she scheduled program administrators in the Cellular, Organ, and Systems Pathobiology Branch (COSPB) and Susceptibility and Population Health Branch (SPHB) as moderators for presentations by their respective grantees:

- Pulmonary Disease and Environmental Factors — COSPB Program Administrator Sri Nadadur, Ph.D.
- Fibrotic Responses to the Environment — Nadadur
- Mechanisms in Nanotoxicology — Nadadur
- Effects of Arsenic Exposure — SPHB Program Administrator Kim McAllister, Ph.D.
- Endocrine Acting Chemical Response — COSPB Chief Jerrold Heindel, Ph.D.
- Mechanisms of Mutagenesis, Carcinogenesis, and DNA Repair — SPHB Program Administrator Dan Shaughnessy, Ph.D.
- Cardiovascular Responses to the Environment — DERT Deputy Director Pat Mastin, Ph.D.
- Mechanisms in Neurotoxicology — COSPB Program Administrator Annette Kirshner, Ph.D.

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# Symposium highlights emerging role of 3D tissue modeling in EHS

By Ernie Hood

Judging from the presentations at the June 27-28 NIEHS workshop, “Engineered Tissue Models for Environmental Health Sciences Research” (see text box), it won’t be long before 3D tissue models are essential tools in risk assessment and environmental health. After decades of basic research, the science and technology underlying these “organs-on-a-chip” are developing rapidly, and the field appears to be poised for translation and commercialization into a variety of applications in toxicology, pharmacology, and medicine.

“We think that this is the future,” said keynote speaker [Donald Ingber, M.D., Ph.D.](#), founding director of the [Wyss Institute for Biologically Inspired Engineering](#) at Harvard University and a pioneer in the field. “I think it can be integrated and have impact quickly... It’s of a scale that it can be manufactured with microchip technologies that are cheap and robust, and the response that we’re getting from the chemical industry, as well as pharma, has been amazing.

## Highlighting new opportunities in biomedical research

The meeting was organized by NIEHS Program Administrator David Balshaw, Ph.D., who said that the gathering had two main goals — to provide a series of presentations to the NIEHS community to showcase leading-edge engineered tissue systems as research tools and to hold an expert discussion panel to provide feedback to NIEHS on how to develop a portfolio in the field.

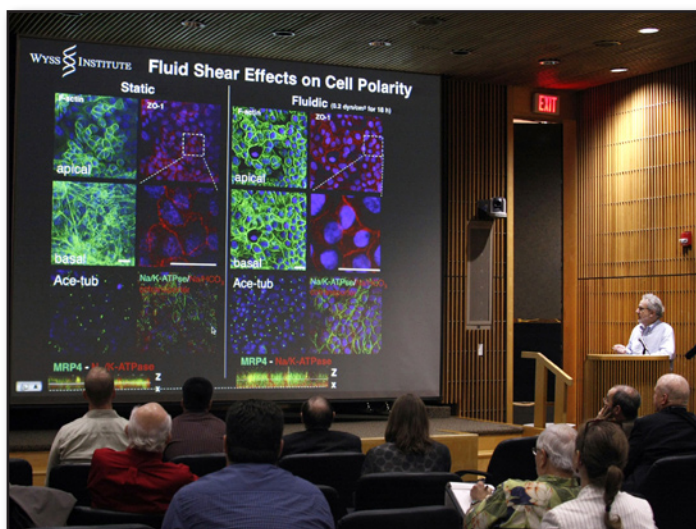
“It was a fantastic day and a half of science,” said Balshaw. “We heard about a variety of models, from well-established tissues like lung and skin to more developmental systems like breast cells, neuronal tissues, and capillary beds. We also talked about the development of computational models and the integration of both wet and computational models into high-throughput screens.”

## Reality check — making models better mimic organisms

Although numerous 2D cell-based systems have traditionally been used to gain information about potential hazards, often findings do not translate well to human biology, because cell culture does not accurately represent



*Ingber described his group’s work at the Wyss Institute and provided an overview of the many exciting developments in the field, as well as an encouraging look at the future potential of 3D tissue modeling. (Photo courtesy of Steve McCaw)*



*Ingber discussed the importance of 3D model systems taking biological forces, such as shear and flow, into account in order to effectively recreate physical conditions in the cell. (Photo courtesy of Steve McCaw)*

many of the structures and functions of normal tissue. The potentially huge advantage of the 3D systems is their power to provide responses that more closely reflect what happens *in vivo*. They incorporate multiple cell types and, in many cases, reflect the fundamental anatomy found in native tissue. They even include cell-cell signaling and biological forces such as stress, strain, and flow as critical aspects of the physiological response to environmental factors.

As NIEHS/NTP Director Linda Birnbaum, Ph.D., explained in her opening comments to attendees, to achieve the desired “biological reality,” several other components are necessary to reflect the complex structures, functions, and even spatial and temporal elements that all combine in a working tissue or organ (see figure on next page). Although many of the needed building blocks already exist, some are still in development, and one of the objectives of the meeting was to assess the current state of the science and identify the engineering, experimental and computational work needed to accelerate progress in the field. As Balshaw put it, “There’s a lot that can be done now, but a lot left to do. Throughput is still moderately low, and many systems still need to be validated. Moving this forward will rely on interdisciplinary teams.”

NTP Biomolecular Screening Branch Chief and Tox21 liaison [Raymond Tice, Ph.D.](#), told participants there were many potential applications of 3D tissue modeling systems to efforts by Tox21, a unique collaboration between several federal agencies to research and test chemicals in a new way.

Not only would it be very useful for 3D systems to test compounds for their effects on organ function, Tice explained, but assessing effects on organ development would also be of great interest. He also said he hopes the models can be used to evaluate gene and compound interactions within and across species, so as to understand differential sensitivity to toxicants and what’s happening at the cell pathway level. “That’s where I think we can make some really great strides,” said Tice.

(Ernie Hood is a contract writer with the NIEHS Office of Communications and Public Liaison.)

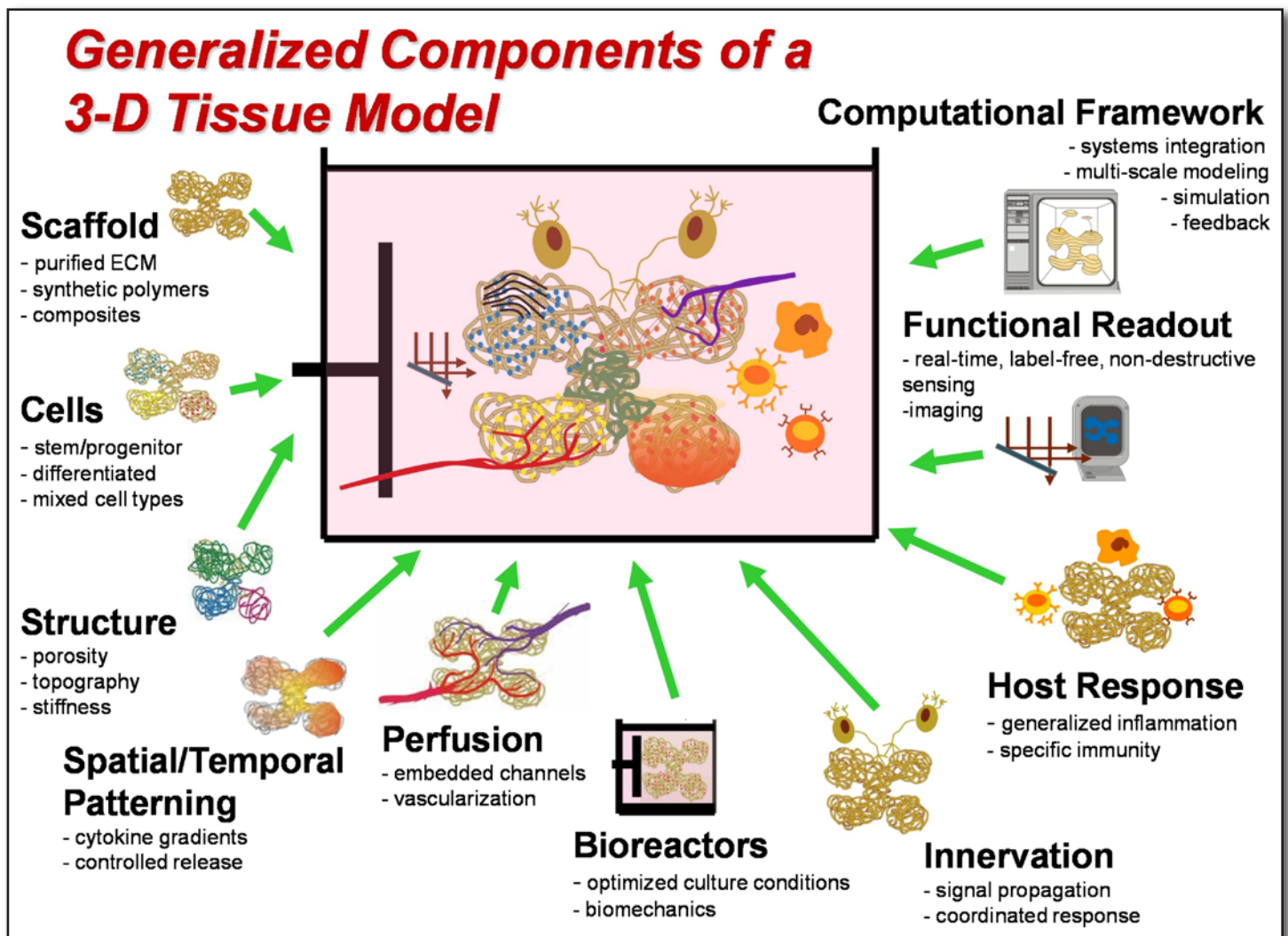


*Superfine described his group’s Virtual Lung Project, which is designed to provide *in vitro* and *in silico* modeling of mucus clearance. (Photo courtesy of Steve McCaw)*



*Tice communicated Tox21’s enthusiasm for 3D tissue modeling approaches to help transform toxicology from an observational to a predictive science, but noted that there is still much research to be conducted before it can reach its full potential. (Photo courtesy of Steve McCaw)*





According to Birnbaum, the combination of these elements is what gives 3D tissue models the power to mimic biological systems more closely than 2D cell cultures. All are not yet perfected, but progress has been swift in recent years. (Slide courtesy of Linda Birnbaum)



Speakers at the conference gathered in front of the Rall Building for a group shot. Shown, left to right, are Superfine, Fritsche, George, Takashima, Herlyn, conference organizer Balshaw, Sonnenschein, Tice, Ingber, and Wambaugh. (Photo courtesy of Steve McCaw)

## Tissue Models on Parade

In addition to Ingber and Tice, each of the speakers at the 3D Tissue Modeling symposium presented science at the very forefront of the field:

- [Richard Superfine, Ph.D.](#), from the University of North Carolina at Chapel Hill presented the Virtual Lung Project, which is a combined experimental and computational modeling exercise. A particular focus is on models of mucociliary clearance that can be used to assess transport and clearance of exposures in the lung.
- [Ellen Fritsche, M.D.](#), of Heinrich-Heine Universität Düsseldorf in Germany works with neurospheres made of human neuroprogenitor cells, which are being used to assess toxicity through AhR, Nrf2 and Thr pathways.
- [Carlos Sonnenschein, M.D.](#), of Tufts University, focuses on modeling the developmental basis of breast cancer. He also spoke to some of the fundamental issues relating to scaffolding and computational analysis of the complex dynamics of systems.
- [John Wambaugh, Ph.D.](#), from the U.S. Environmental Protection Agency National Center for Computational Toxicology spoke about the virtual liver and virtual embryo computational modeling projects being developed within EPA. These computational screens are a powerful supplement to the Tox21 screening effort.
- [Steven George, M.D., Ph.D.](#), from the University of California, Irvine spoke about his microtissue vascularization effort, which is developing a system to form capillary beds within tissue arrays, adding an additional level of physiological relevance to engineered tissue models.
- [Meenhard Herlyn, D.V.M., D.Sc.](#), from the Wistar Cancer Institute spoke about the multi-cellular skin model that is being used to examine cellular transformation in skin cancer and in efforts to derive the model from induced pluripotent stem (iPS) cells.
- [Akira Takashima, M.D., Ph.D.](#), from the University of Toledo, spoke about his group's multi-cellular skin model for assessing irritant and allergic dermatitis as a moderate- to high-throughput screen for potential toxicants.

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## Using nutrition to alter host susceptibility to environmental toxicants

*By Emily Zhou*

As part of the Superfund Research Program (SRP) Distinguished Lecturer Series, nutritional toxicologist [Bernhard Hennig, Ph.D.](#), of the University of Kentucky (UK), discussed ways to attenuate vascular endothelial cell dysfunction induced by exposure to polychlorinated biphenyls (PCBs) during a seminar July 14 at NIEHS. Hennig offered a compelling argument for using nutritional modulation of environmental insults in vasculature-related diseases and educating people about ways to improve their nutritional status.



“Nutritional interventions may provide the most sensible means to develop primary prevention strategies for diseases associated with many environmental toxic insults,” Hennig maintained, including such major public health concerns as atherosclerosis and type 2 diabetes.

Building on this nutritional paradigm, Hennig advocates for what he calls “a mindful nutrition,” including healthy diet and a regular exercise routine, as key to countering the effects of genetic predisposition to disease and exposure to environmental pollutants. Although people can’t control their genetic makeup and aren’t always aware of toxicants in their environments, Hennig said, “We can control our lifestyles.”

Hennig is the director of the SRP-funded [Nutrition and Superfund Chemical Toxicity \(NSCT\) program](#) at UK, which manages biomedical and environmental engineering projects that interact with the research translation core for community outreach and education. The program’s community engagement activities include translating nutrition research to public with registered dietitians — promoting a healthy diet of more fruits, vegetables, fiber, and low-fat foods to boost immune system, as well as more physical activity.



*In response to a question by NIEHS/NTP Director Linda Birnbaum, Ph.D., about whether early life PCB exposure would predispose for development of diabetes and cardiovascular diseases, Hennig said, “There is lots of interest in looking at this, and experiments are underway.” (Photo courtesy of Steve McCaw)*

### **PCBs and atherosclerosis — What are the mechanisms?**

As Hennig explained, research at the NSCT program showed that PCBs induce adipocyte differentiation and expression of proinflammatory cytokines in adipocytes. In addition, in experiments with mice, PCBs promote glucose and insulin intolerance associated with dysregulation of cytokine messages and protein levels. Only recently, however, have researchers established that PCB exposure also contributes to vascular diseases, showing that persistent organic pollutants, such as PCBs, can lead to cardiovascular toxicity and atherosclerosis.

Arylhydrocarbon receptor (AhR) and its subsequent activation by AhR ligands, such as coplanar PCBs, mediate gene expression in the nucleus that generates reactive oxygen species (ROS) and thereby induces expression of proinflammatory cytokines, including interleukins (IL), nuclear factor kappa-light-chain-enhancer of activated B cells (NF- $\kappa$ B), and vascular cell adhesion protein (VCAM). In doing so, AhR ligands are atherogenic and disrupt barrier functions of endothelial cells by increasing transendothelial flux in blood vessels.

Hennig also explained that caveolin-1 (cav-1) was found to be a culprit in exacerbating PCB-induced inflammatory responses. PCB exposure leads to upregulation of cav-1 protein expression. Cav-1 binds AhR in co-immunoprecipitation assay, and PCB exposure magnifies this interaction.



*Heather Henry, Ph.D., program administrator for the NIEHS SRP, was host of Hennig’s seminar. She listened intently to his argument that nutrition interventions can pave the way for developing primary prevention strategies of diseases associated with many environmental toxic insults. (Photo courtesy of Steve McCaw)*

## Nutrition as a preventive measure against environmental chemical toxicity

Hennig's laboratory showed that omega-3 polyunsaturated fatty acids block PCB-mediated oxidative stress, and downregulate inflammation in both cell culture studies and in animal models. In contrast, omega-6 fatty acids, found in many edible fats, such as corn or safflower oils, amplify PCB-induced inflammation and, even by themselves, induce lower-grade inflammation. In addition, flavonoids, such as quercetin polyphenols, block PCB induction of cav-1 protein expression.

Hennig explained that it's difficult to specify the optimal amount of omega-3 intake, but he suggested that a close to 1 to 1 ratio of omega-6 to omega-3 is very good. "The [typical] American diet is composed of about a 10 to 1 ratio of omega-6 to omega-3," said Hennig.

Hennig also noted that he is exploring the potential of cav-1 as a biomarker for diagnosis of atherosclerosis induced by environmental pollutants. He said the use of tissues or body fluids for this screen is currently under investigation.

(Emily Zhou, Ph.D., is a Research Fellow in the NIEHS Laboratory of Signal Transduction Inositol Signaling Group.)

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*NIEHS SRP founder and Director Bill Suk, Ph.D., joined Hennig following the presentation. As Suk commented at an earlier workshop at UK in January 2011, "It's clear that nutrition can be a potential modulator of diseases that have been associated with exposure to environmental stressors, and this interplay will have important implications in risk assessment." (Photo courtesy of Steve McCaw)*

### Community awareness and education

Hennig and his NSCT program staff work together to pinpoint the science behind the interplay among environmental toxins, nutrition, and disease. They are also dedicated to raising the public awareness of their research results in their communities. Their projects are nicely integrated with their Community Outreach and Research Translation Cores, which have reached out to numerous communities, including ones near PCB-contaminated Superfund sites in Paducah and Harlan County, Ky., to educate residents about the importance of diet for overall health and protection against the harmful effects of exposure to pollutants. NSCT, Hennig said, also collaborates with the state's Cooperative Extension Service, which is also based at the university.

## Study links phthalate and BPA exposure to altered thyroid signaling in humans

*By Ian Thomas*

A new [study](#) by NIEHS grantees has uncovered strong evidence supporting the theory that increased exposure to certain chemicals found in ordinary plastics could lead to irregular thyroid signaling in humans, a known cause of many serious health risks, including excessive weight gain.

Utilizing data from the CDC's National Health and Nutrition Examination Survey (NHANES), researchers from the University of Michigan analyzed biomarker and survey information from more than 1,600 subjects,



in search of a connection between thyroid hormone levels and exposure to phthalate and bisphenol A (BPA), both components of an array of everyday products, such as plastic drinking bottles.

“Phthalates and BPA have been associated with a range of adverse health outcomes, many of which may be mediated through altered thyroid signaling,” said [John Meeker, Sc.D.](#), the principal investigator on the study. “The goal of this analysis was to explore whether we would find associations between these chemicals and thyroid measures consistent with those that we reported previously in a smaller study among adult men.”

### Gaining the power of numbers

By cross-referencing urinary exposure-biomarker concentrations with serum thyroid measures and a number of important covariates from 1,346 adults, age 20 or older, and 329 adolescents, age 12 to 19, Meeker and his co-author, graduate student Kelly Ferguson, looked for changes in the thyroid function measures associated with various levels of chemical exposure.

“Among adults, we found that higher concentrations of metabolites of di(2-ethylhexyl) phthalate (DEHP) in urine were associated with decreased thyroid hormone levels in blood,” he explained. “These results were, for the most part, consistent with our previous reports among adult men. We did not find the same relationships among adolescents, though the number of participants was much smaller in that age group.”

While previous studies have been conducted on this topic, most in animal, in vitro, and some limited human models, what makes this investigation unique is its large sample of human subjects, due to its usage of 2007-2008 NHANES data.

Launched in the early 1960s as a series of surveys to foster a better understanding of the general public health, the NHANES program evolved in 1999 into a continuous study dedicated to assessing the overall health and nutritional status of adults and children in the United States. As a major part of the CDC’s National Center for Health Statistics, NHANES utilizes interview and physical examinations in research derived from a nationally representative sample of roughly 5,000 persons each year.

“Since our original work on this topic was limited to a small group of men attending a fertility clinic, there was a bit of uncertainty surrounding our ability to generalize the findings to broader populations,” Meeker explained. “This analysis, among a representative sample of the U.S. general population, goes a long way in strengthening the case for these exposure-response relationships, though at the same time, it may also serve to support the generalizability of our findings from the fertility study.”



*Meeker completed his doctorate of science in exposure, epidemiology, and risk from Harvard University in 2004. His latest study was funded by [NIEHS](#) and the U.S. Environmental Protection Agency. (Photo courtesy of John Meeker)*



*Ferguson is a Ph.D. student in environmental health sciences at the University of Michigan, School of Public Health. (Photo courtesy of Kelly Ferguson)*

## Moving forward with additional laboratory and population studies

The authors agree that while the outcome of this study may offer clues about the relationship between phthalate and BPA exposure and altered thyroid signaling, a great deal of additional research must be done before these products begin disappearing from supermarket shelves. In the meantime, Meeker and his colleagues are firmly committed to knowing everything they can.

Meeker said that he and his colleagues are conducting several ongoing studies to assess the effects of these chemicals in a number of different areas, from reproductive health to pregnancy outcome and child growth and development. “Altered thyroid signaling could very well prove to be an important biological pathway in the relationship between environmental exposures and health outcomes,” he noted. “Therefore, through collaborations with other scientists using laboratory-based experimental research, along with other epidemiologic approaches like this, we plan on exploring that possibility.”

*Citation:* [Meeker JD, Ferguson KK](#). 2011. Relationship between urinary phthalate and bisphenol A concentrations and serum thyroid measures in U.S. adults and adolescents from NHANES 2007-08. *Environ Health Perspect*; doi:10.1289/ehp.1103582; [Online 11 July 2011].

(Ian Thomas is a writer/editor in the NIEHS Office of Communication and Public Liaison)

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## Journal features Jean Harry article

*By Robin Arnette*

In a new initiative to promote innovative research conducted in neuroscience, behavioral studies, and immunology, the journal *Brain, Behavior, and Immunity* will issue a press release that highlights an article by [Jean Harry, Ph.D.](#) The article, titled “Voluntary exercise protects hippocampal neurons from trimethyltin injury: Possible role of interleukin-6 to modulate tumor necrosis factor receptor-mediated neurotoxicity,” appeared online in the journal on March 22.

Harry’s paper is the first article from the journal to receive targeted publicity, which corresponds with the August print issue of *Brain, Behavior, and Immunity*.

Harry is a principal investigator in the Laboratory of Toxicology and Pharmacology [Neurotoxicology Group](#). Her findings suggest that interleukin-6, an anti-inflammatory factor, plays a dual role in the prevention of damage and associated seizures, as well as in promoting repair after brain injury. For more on this exciting work, see an [overview](#) of the research from the May issue of the *Environmental Factor*.



*Harry is principal investigator on the new study, leading a team of scientists from NIEHS and a former group member who is now with the University of Alabama at Birmingham. (Photo courtesy of Steve McCaw)*

Founded in 1987, [Brain, Behavior, and Immunity](#) is the official journal of the Psychoneuroimmunology Research Society. It is an international, interdisciplinary journal that publishes peer-reviewed basic, experimental, and clinical studies dealing with behavioral, neural, endocrine, and immune system interactions in humans and animals.



*Citation:* Funk JA, Gohlke J, Kraft AD, McPherson CA, Collins JB, Harry GJ. 2011. Voluntary exercise protects hippocampal neurons from trimethyltin injury: Possible role of interleukin-6 to modulate tumor necrosis factor receptor-mediated neurotoxicity. *Brain Behav Immun*; 25(6):1063-1077.

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## NIEHS investigators discover new mechanism in learning and memory

*By Robin Arnette*

New findings in mice, published by NIEHS researchers, suggest that the timing of neurotransmitter acetylcholine release in the brain's hippocampus may play a key role in regulating the strength of nerve cell connections, called synapses. Understanding the complex nature of neuronal signaling at synapses could lead to better understanding of learning and memory, and novel treatments for relevant disorders, such as Alzheimer's disease and schizophrenia.

Neurons in the hippocampus, one of the parts of the brain that is thought to have a critical function in learning and memory, communicate with each other at synapses by releasing various neurotransmitters, including acetylcholine and glutamate, which stimulate electrical signals in the adjacent neurons.

For years, neuroscientists have been working to determine which cellular processes allow humans to learn from experience and store memories, and how these processes are compromised by conditions such as schizophrenia and Alzheimer's disease. Now, researchers at NIEHS believe they have found one such mechanism for synchronizing changes in the strength of synapses. The results of the [study](#) were published online July 13 in the journal *Neuron*.



*Lead author Yakel has led the Ion Channel Physiology Group ever since he joined the Laboratory of Neurobiology in 1993. (Photo courtesy of Steve McCaw)*

### Timing may be key

"We've demonstrated that when we stimulate the release of acetylcholine at just the right time in the hippocampus, we can induce a cellular change at synapses that use glutamate," said [Jerrel Yakel, Ph.D.](#), a senior investigator in the NIEHS Laboratory of Neurobiology and co-author of the paper.

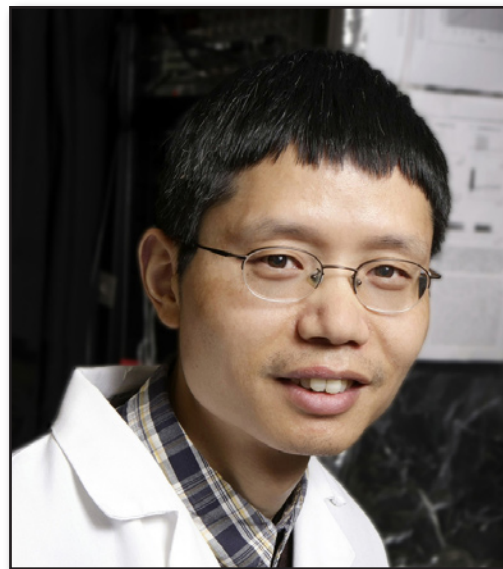
Previous work by other researchers had established that learning and memory are mediated by the strengthening or weakening of synapses, where electrical signals that last less than a hundredth of a second release neurotransmitters that change the electrical impulses of the connected neurons. In this study, Yakel and [Zhenglin Gu, Ph.D.](#), a research fellow in Yakel's group and co-author of the publication, used molecular biology techniques to get some of the neurons in mouse brain cells to produce a special light-sensitive protein, and then used a laser to stimulate these neurons to release acetylcholine.

"A change of even a few hundredths of a second in the timing of acetylcholine release can make a difference," said Gu. "No one had shown this was important until now."

Yakel said the findings are also a potentially important step in the study of disorders that affect learning and memory, such as Alzheimer's disease and schizophrenia, where the acetylcholine system and hippocampus are known to play critical roles. For example, amyloid beta peptide is the major component of plaques that form in the brains of Alzheimer's patients and is thought to participate in the memory loss associated with Alzheimer's disease. In this report, Yakel and Gu expand upon earlier findings that amyloid beta peptide disrupts acetylcholine's ability to regulate synaptic strength.

*Citation:* Citation: [Gu Z, Yakel JL](#). 2011. Timing-dependent septal cholinergic induction of dynamic hippocampal synaptic plasticity. *Neuron* 14;71(1):155-165.

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*First author Gu (Photo courtesy of Steve McCaw)*

## New study explores the unexpected interface of RNA and DNA

*By Robin Arnette*

A group of NIEHS researchers, led by Thomas Kunkel, Ph.D., recently made a surprising find. They demonstrated that the enzymes in yeast that replicate or copy DNA in eukaryotes incorporate lots of ribonucleotides, which are normally part of RNA, not DNA.

Kunkel's results appeared [online](#) in the March 1, 2010 issue of the *Proceedings of the National Academy of Sciences (PNAS)*, but the article raised more questions, which Kunkel pursued in his latest [work](#), published in the June 24 issue of *Science*.

[Kunkel](#) was intrigued by the implications of having ribonucleotides involved in DNA replication stability. For instance, since ribonucleotides are sensitive to strand breakage, did the presence of ribonucleotides in DNA lead to mutagenesis or genome instability? The answers had potential implications for understanding the origins of human disease, so Kunkel was compelled to keep digging for clues.

His latest study showed that removing the ability of yeast cells to get rid of ribonucleotides in DNA creates an uncommon mutation in the DNA, but the mutation could be abolished if the activity of topoisomerase 1 (Top1), an enzyme that maintains the integrity of DNA, was lost. This novel breakthrough not only has implications for cancer research; it also fosters a new way of thinking about the possible causes of a rare autoimmune disease called [Aicardi Goutières syndrome](#) and perhaps other autoimmune disorders.

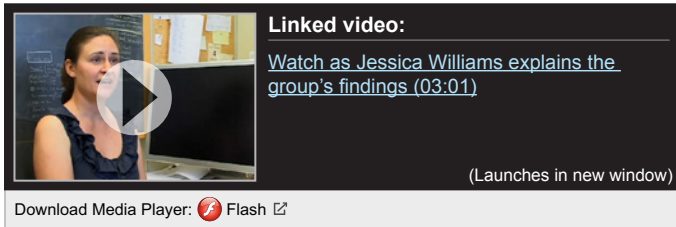


*Kunkel is a principal investigator in the NIEHS Laboratory of Molecular Genetics and chief of the Laboratory of Structural Biology. He said that finding ribonucleotides in DNA as a cause by which mutations arise in the genome was a novel finding that took everyone by surprise. (Photo courtesy of Steve McCaw)*



## RNase H2 and Top1

Kunkel's research fellow, Jessica Williams, Ph.D., and biologist Alan Clark, constructed two strains in budding yeast. In one strain, they deleted the gene that encodes the catalytic subunit of RNase H2, a key enzyme that removes ribonucleotides from DNA. In the other, they deleted the genes for RNase H2 and Top1. Using a reporter system that monitored spontaneous mutations that occur in DNA, they found that the yeast lacking RNase H2 exhibited short, unusual 2-5 base pair deletions in repetitive sequences. However, the strain missing both RNase H2 and Top1 didn't display these mutations. The data suggested that the deletions were due to the activity of Top1.



"These results are meaningful because chemicals that inhibit Top1 activity are used as anti-cancer agents, and mutations in the RNase H2 enzyme have been identified in patients with Aicardi Goutières syndrome," Williams said.

## Peeling the research onion

Just like Kunkel's PNAS article and subsequent papers, these findings pose more questions. He said a few obvious inquiries come to mind. Are ribonucleotides in DNA involved in tumor formation? Do ribonucleotides in DNA have a signaling function? Are there additional DNA repair pathways outside of RNase H2 that process ribonucleotides in DNA? His group is currently examining several of these ideas.

"The cell could have many things going on that depend on ribonucleotides in DNA that no one has explored," Kunkel noted.

## Two worlds of thought come together

Although Kunkel's studies on ribonucleotides in DNA laid the groundwork for this article, his collaborators, [Sue Jinks-Robertson, Ph.D.](#), of Duke University, and [Yves Pommier, M.D., Ph.D.](#), of NIH's National Cancer Institute, also uncovered key data. Jinks-Robertson's previously published work generated the same rare 2-5 base pair deletion in yeast, but the culprit wasn't ribonucleotides in DNA; rather it correlated with a high level of gene transcription known as transcription-associated mutagenesis. Since these deletions depended on Top1 activity, her group investigated a likely connection between ribonucleotides and Top1.



*"Although the idea is pure speculation at the moment, it's conceivable that RNase H2 defects are also relevant to autoimmunity in general," Williams added. (Photo courtesy of Steve McCaw)*



*Alan Clark is a co-author on the article published in Science magazine. (Photo courtesy of Steve McCaw)*

As a specialist in topoisomerases, Pommier provided direct biochemical evidence that Top1 cleaves at the site of a ribonucleotide causing a break in the DNA, which can lead to the deletion mutations observed in the yeast strains.

Kunkel said the thing that excited him the most about the Science paper was the linkage between DNA replication and transcription. Experts in both fields now need to pay attention to the scientific connections between the two. He summed up his feelings by saying, “[This work] is at this interface between two very big efforts in research by people who don’t normally pay a lot of attention to each other. To me, discoveries are made at these kinds of interfaces.”

*Citation:* [Kim N, Huang SY, Williams JS, Li YC, Clark AB, Cho JE, Kunkel TA, Pommier Y, Jinks-Robertson S. 2011. Mutagenic processing of ribonucleotides in DNA by yeast topoisomerase 1. Science 332\(6037\):1561-1564.](#)

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## New journal makes surprising impact in first year of publication

*By Eddy Ball*

A cross-disciplinary journal with ties to a program funded by NIEHS since 1992 has achieved one of the highest impact factors of specialized journals of its type at 3.592, according to the 2010 Thomson Reuters Journal Citation Reports (JCR).

An NIEHS [grant](#) to the [University of Cincinnati \(UC\) Center for Environmental Genetics \(CEG\)](#) has funded research into the effects of chemical trace elements on biological systems and health by UC Professor Joseph Caruso, Ph.D., a long-time CEG member and founding and editorial board member of the journal [Metallomics](#), which began publishing in 2009.

### A new omics approach to analyzing metal complexes

According to a 2008 [article](#) in Highlights in Chemical Biology by Ryszard Lobinski, Ph.D., D.Sc., and colleagues at the National Research Council of France, metallomics helps fill an important gap in omics studies of biological systems. “Metallomics is the systematic study of metallomes [metal complexes] and the interactions and functional connections of metal ions and their species with genes, proteins, metabolites, and other biomolecules within organisms and ecosystems,” Lobinski wrote. Moving beyond investigations of the role and interactions of a single, or even few, metals in a protein or enzyme system, metallomics purports to study global, multi-element interactions, and relationships.

Caruso has been a leader of efforts to bring together scientists from the biological, chemical, environmental, clinical, and measurement sciences, to effect a greater understanding of the role of metals and metal compounds in many biological, chemical, environmental, and clinical systems. He has been a featured speaker at the biennial [International Symposium on Metallomics](#). Caruso founded and directs the UC/Agilent Technologies Metallomics Center of the Americas, established in 2007.



*Metallomics developer and founder of the new journal, Joe Caruso (Photo courtesy of Joseph Caruso)*



## Putting impact factors into perspective

Metallomics' impact factor surpasses such journals as the Journal of Biological Inorganic Chemistry at 3.287 and Biometals at 2.320. According to Caruso, the journal's performance is even more impressive because the impact factor ranking is based solely on 2010 citations to the initial six issues published in 2009. Metallomics is currently indexed in PubMed and Scopus.

JCR impact reports are useful for libraries, publishers, authors, researchers, and information analysts in assessing the impact, immediacy, and total cites for specific journals.

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## With support from NIEHS

Caruso has collaborated on a number of multidisciplinary publications with other CEG members, and many of the projects were supported by the NIEHS center grant. A recent publication, supported with pilot project funding from NIEHS, utilized arsenic speciation and quantification analyses conducted at the University of Cincinnati/Agilent Technologies Metallomics Center of the Americas.

*Citation:* [Muñiz Ortiz JG](#), [Shang J](#), [Catron B](#), [Landerio J](#), [Caruso JA](#), [Cartwright IL](#). 2011. A transgenic Drosophila model for arsenic methylation suggests a metabolic rationale for differential dose-dependent toxicity endpoints. *Toxicol Sci* 121(2):303-311.

## Ribonucleotide incorporation into DNA study honored by JBC

*By Jeffrey Stumpf*

Research from the NIEHS Laboratory of Structural Biology (LSB) provides the latest chapter in the story of a rapidly growing field that investigates the role of ribonucleotide incorporation into DNA and how these basic processes may affect the health of an organism and its response to endogenous cellular metabolism or exposure to the environment.

In July, the Journal of Biological Chemistry (JBC) honored a new [study](#) by LSB investigators on the biochemical and structural characterization of ribonucleotide incorporation by human DNA polymerase beta (pol beta) by naming it Paper of the Week. JBC associate editors and editorial board members bestow this honor on the top one percent of papers reviewed in terms of significance and overall importance, according to the JBC website.

A fundamental role of DNA polymerases is to insert the correct deoxyribonucleoside triphosphate (dNTP) opposite a DNA template, discriminating against an incorrect base or ribonucleoside triphosphate (rNTP). However, members of the LSB DNA Repair and Nucleic Acid Enzymology Group, headed by [Samuel Wilson, M.D.](#), are the latest to show that polymerases can introduce ribonucleotides frequently during DNA replication, as much as two percent of the time for pol beta. Although the biological consequences are unknown, lead author [Nisha Cavanaugh, Ph.D.](#),



*In his roles as a leader and researcher at NIEHS, Wilson has long championed research on the role of DNA pol beta in DNA repair and replication. As principal investigator on the study, Wilson led a multifaceted approach toward understanding the enzyme that involved a collaborative effort between members of his own group — William Beard, Ph.D., Vinod Batra, Ph.D., Cavanaugh, and David Shock — and members of the LSB Computational Chemistry and Molecular Modeling Group — head Lee Pedersen, Ph.D., and Lalith Perera, Ph.D. (Photo courtesy of Steve McCaw)*

a postdoctoral fellow in the group, said she suspects that limiting rNTP incorporation may be important for normal cell survival.

“Because ribonucleotides are susceptible to hydrolysis, their presence in the genome will result in DNA strand breaks and genome instability,” noted Cavanaugh. “Additionally, rNTP incorporation may disrupt nucleic acid binding proteins, such as transcription factors, that rely on specific sequences or conformations.”

### Potential clinical implications

Ribonucleotides vastly outnumber dNTPs in growing cells, allowing for higher probability of rNTP incorporation into DNA. While the majority of the DNA replication field focuses on the study of incorporating the correct base, Wilson points out that sugar-modified nucleosides, such as AZT and araC, are used in the clinic for development of cancer therapies.

“Many aspects toward understanding mechanistic features of the cytotoxic activity of these compounds are poorly understood, and this field represents a really fascinating area for future investigation,” predicted Wilson.

Structural and kinetic studies of nucleotide incorporation by polymerases are key to this investigation.

“By understanding how DNA polymerases discriminate against sugar or base analogs, we can develop better therapeutic nucleotide analogs that could target specific DNA polymerases,” added Cavanaugh.

### Good fences make good polymerases

Pol beta fills short gaps that result from the process that repairs simple DNA lesions, called base excision repair. Similar to other DNA polymerases, pol beta discriminates against rNTP incorporation using an important tyrosine residue 271 (Tyr-271), whose side chain and peptide backbone carbonyl forms a steric fence. Different polymerases contain different steric gate residues, but the importance of this variation on rNTP incorporation is unknown.

The researchers purified mutant pol beta where tyrosine was substituted with alanine (Y271A), thus eliminating the majority of the side chain. By determining the three-dimensional structure of the Y271A mutant bound to DNA and the incorporated rNTP, the authors realized that both the tyrosine backbone and the side chain inhibit rNTP incorporation, prompting the comparison to a steric fence rather than just a gate.

Landscaping aside, at least two other factors influence rNTP incorporation. Structural data suggest a hydrogen bond between the side chain of Tyr-271 and the primer terminus that may provide a geometry that discriminates against ribonucleotides. Also, kinetic analyses show that substituting manganese for magnesium as the chelating metal ion increases rNTP binding affinity 200-fold. However, Cavanaugh asserts that adjustments of the reactive atoms in the active site that deter ribonucleotide insertion are subtle.

“The crystallographic structure of pol beta indicates that the ribonucleotide is well accommodated,” observed Cavanaugh. “This data contributes to the mechanism that explains why pol Beta inserts ribonucleotides much more often than deoxyribonucleotides with the wrong base.”



*Cavanaugh was the first author on the JBC paper of the week. Her research was also honored by NIH with a Fellows Award for Research Excellence. (Photo courtesy of Steve McCaw)*



## Paper expands NIEHS interest in rNTPs incorporation into DNA

Recent emerging interest by NIEHS researchers in ribonucleotide incorporation into DNA reflects the importance of this work to environmental health and disease. Although this subject has lacked sufficient investigation throughout the decades of mutagenesis research, the importance of DNA repair of ribonucleotides is now evident.

Leading the charge is LSB Chief Thomas Kunkel, Ph.D., whose lab uses biochemical and genetic tools to measure the effects of ribonucleotide incorporation into DNA. He notes that the disease relevance is already there. “RNase H2 initiates repair of ribonucleotides in DNA, and mutations in the genes encoding the three subunits of human RNase H2 are causally associated with Aicardi-Goutières syndrome,” stated Kunkel.

Mitochondrial DNA is not immune to ribonucleotide incorporation, which may cause mitochondrial disease. Chief of the Laboratory of Molecular Genetics William Copeland, Ph.D., is leading studies into how the mitochondrial DNA polymerase (pol gamma) discriminates against rNTPs. “We have already observed mitochondrial patients with mutant pol gamma that exhibits a loss of ribonucleotide discrimination,” said Copeland.

*Citation:* [Cavanaugh NA](#), [Beard WA](#), [Batra VK](#), [Perera L](#), [Pedersen LG](#), [Wilson SH](#). 2011. Molecular insights into DNA polymerase deterrents for ribonucleotide insertion. *J Biol Chem*; doi/10.1074/jbc.M111.253401 [Online 6 July 2011].

(Jeffrey Stumpf, Ph.D., is a postdoctoral fellow in the NIEHS Laboratory of Molecular Genetics Mitochondrial DNA Replication Group.)

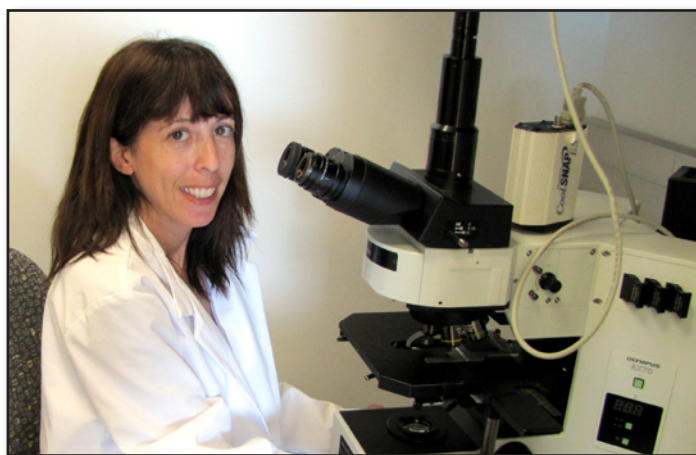
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## Study finds BPA-exposed male deer mice less attractive to females

*By Thaddeus Schug*

In a new study, published June 27, NIEHS-funded investigators add to the ongoing debate surrounding the safety of products made with the chemical bisphenol A (BPA). With BPA studies having varying results and interpretations, experts are still uncertain about what these results mean to human health.

NIEHS grantee [Cheryl Rosenfeld, Ph.D., D.V.M.](#), and her group at the University of Missouri-Columbia (UM), who report that male deer mice whose mothers were fed a diet containing BPA while pregnant are subtly, yet significantly, different from males with no BPA exposure. The BPA-exposed mice exhibit traits indicating decreased masculinity and learning ability, differences that could impair their mating behaviors and their likelihood of producing offspring.



*According to Rosenfeld, BPA exposure through the diet has been underestimated by previous lab tests. “We believe that these mouse model studies are a more accurate representation of what happens to BPA as the human body attempts to process this toxic substance.” (Photo courtesy of Cheryl Rosenfeld)*

In the [study](#), BPA-exposed male deer mice were unable to navigate their way out of a maze, even though their untainted male peers quickly mastered the same maze. By a two-to-one margin, female deer mice showed less sexual interest in BPA-affected males compared to unexposed males.

“The BPA-exposed deer mice in our study look normal; there is nothing obviously wrong with them. Yet, they are clearly different,” said Cheryl Rosenfeld, associate professor of biomedical sciences in the College of Veterinary Medicine and investigator in the Bond Life Sciences Center. “Females do not want to mate with BPA-exposed male deer mice, and BPA-exposed males perform worse on spatial navigation tasks that assess their ability to find female partners in the wild.”

BPA is one of the most widely produced chemicals in the world, resulting in widespread exposure of humans to this chemical. BPA is used in the manufacturing of polycarbonate plastics, epoxy resins, and flame retardants. Exposure to BPA occurs through many sources, including reusable water bottles, baby bottles, metallic food cans, thermal paper, carbonless copy paper, and consumer electronics, including computers, cell phones, and video game consoles.



*According to the study, a mouse's luck finding a soul mate may depend on the mother's dietary exposure to BPA. (Photo courtesy of Cheryl Rosenfeld)*

### **Addressing the controversy surrounding BPA**

In 2008, the NTP announced that it had “some concern” about the potential negative effects BPA may have on developing children, based on a thorough review of academic and regulatory studies. The current acceptable limit of BPA exposure set by FDA is 50 micrograms per kilogram of weight per day for humans, but animal studies show that chronic exposure to lower levels has effects on biological processes in first- and second-generation offspring, which has prompted a reevaluation of this acceptable limit.

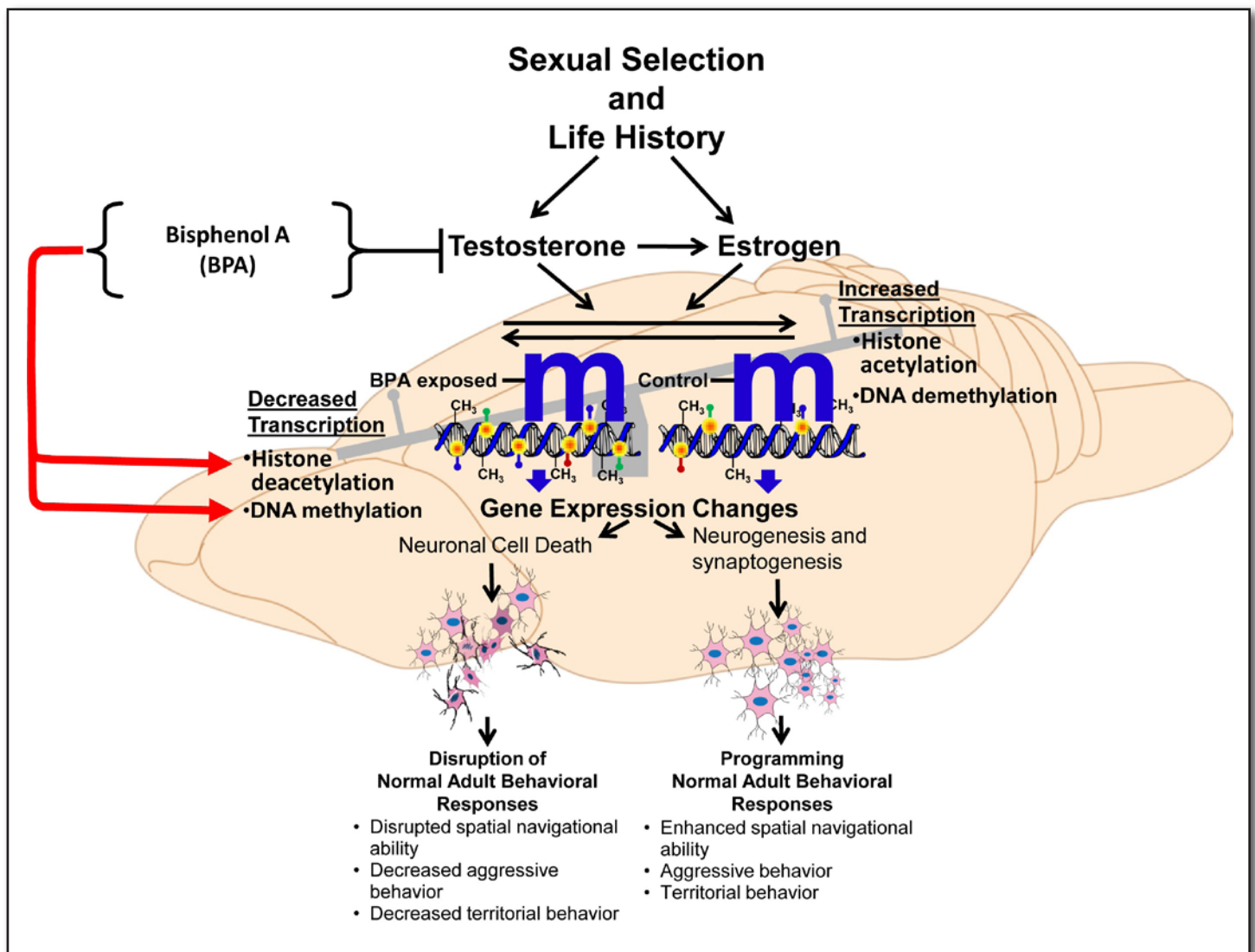
In response to the many inconsistencies in studies involving BPA and growing public concern over its potential to act as a hormone mimic, NIEHS has invested heavily in research related to BPA and other endocrine disrupting chemicals. In 2009, NIEHS awarded 11 BPA Grand Opportunities and Challenge grants, and currently funds a total of 35 projects studying the health effects and risks associated with BPA exposure. The overall goal of these efforts is to sponsor scientifically sound studies on a wide range of BPA-related health concerns, in both animal and human models, that can be used to enhance regulatory decision-making.

According to Jerry Heindel, Ph.D., program administrator and branch chief in the NIEHS Division of Extramural Research and Training (DERT), who oversees much of the Institute's grants portfolio on BPA, work by Rosenfeld, along with the many other current BPA-related studies sponsored by NIEHS, may put to rest many of the controversies surrounding BPA and other endocrine disrupting chemicals. “Cheryl's work adds to the list of over 20 studies showing adverse effects of BPA on some aspect of brain function and significantly expands the data demonstrating changes in one sex more than the other. Thus, we are getting consistent results across labs. I expect to see clarity over the next year from the work of the scientists in the NIEHS-funded BPA consortium,” said Heindel.

In the days ahead, researchers will be trying to refine animal and epidemiological studies for more insight into whether the compound is a harmless chemical, as some studies have found, or a potential threat to human health.

The lead author of the paper, which was published in the June issue of the *Proceedings of the National Academy of Sciences*, was Eldin Jasarevic, a graduate student in the MU Interdisciplinary Neurosciences Program.





Model explaining how daily exposure to BPA prevents the normal estradiol-induced increase in synapses in the hippocampus and prefrontal cortex of nonhuman primates, which could in turn impair cognition. (Graphic courtesy of Cheryl Rosenfeld)

Citation: Jasarevic E, Sieli PT, Twellman EE, Welsh TH Jr, Schachtman TR, Roberts RM, Geary DC, Rosenfeld CS. 2011. Disruption of adult expression of sexually selected traits by developmental exposure to bisphenol A. Proc Natl Acad Sci U S A. 108(28):11715-20.

(Thaddeus Schug, Ph.D., is a postdoctoral research fellow in the NIEHS Laboratory of Signal Transduction and a regular contributor to the Environmental Factor. He is currently on detail as a program analyst in the NIEHS Division of Extramural Research and Training.)

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# Designing a human RNA-binding domain outlined in JBC paper of the week

By Robin Arnette

NIEHS principal investigator [Traci Hall, Ph.D.](#), is interested in how a family of proteins, called PUF RNA-binding domains, recognizes RNA targets. The name PUF was derived from the fruit fly *Drosophila* Pumilio protein and roundworm *Caenorhabditis elegans* fem-3 mRNA binding factor (FBF), and hints at the proteins' universality and importance to living systems.

Starting 10 years ago, Hall's group with Phillip Zamore, Ph.D., at the University of Massachusetts Medical School, determined the first crystal structures of a human PUF protein, quickly followed by structures using RNA targets from the fly version, since human target RNAs had not been identified. Earlier this year, they published work with details on how it recognizes targets in human sequences and in the June 8 [online](#) issue of the Journal of Biological Chemistry (JBC), they published an article that is the culmination of studies to design specific RNA-binding domains. The article has also been selected as the paper of the week and is featured in the July 29 hardcopy issue of the journal.

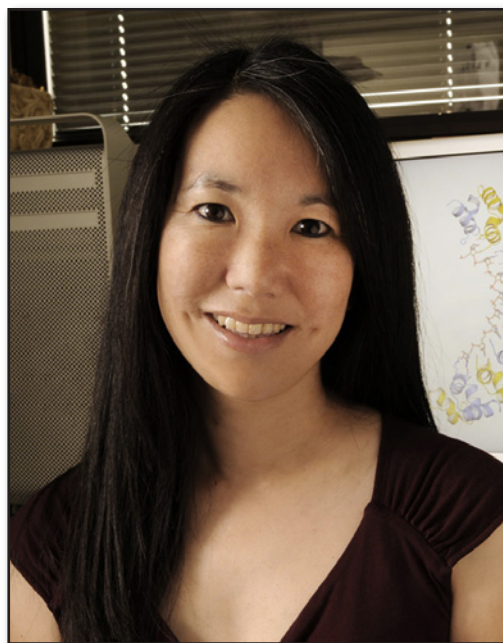
Hall said the reason why her lab studies RNA-binding domains is that these proteins are important factors in gene regulation and can help researchers understand how the environment impacts human health. She said the findings in her latest study, which were made possible by her use of leading-edge three-dimensional imaging in the NIEHS Laboratory of Structural Biology, may also have clinical applications in the fight against cancer ([see text box](#)).

"A key strategy is identifying the pathways that allow our bodies to respond at the molecular level," Hall said. "Without this basic knowledge, it's difficult to determine how the environment interferes with these pathways and how we might combat negative consequences."

## PUF the magic shape sorter

Hall said an illustration of how these proteins work would be to think about it as a sophisticated shape sorter. Imagine the PUF RNA-binding domain possesses a line of connected pockets shaped like circles, squares, and triangles, and the RNAs that bind to it are chains of these shapes. If the pockets on the contraption match the shapes on the RNA, then it has a proper fit and the RNA grabs on. If one shape doesn't match, then the contraption can ignore it and look for another RNA that does match.

However, Hall added, if the PUF RNA-binding domain came across a hexagon, it wouldn't have a pocket that specifically fit that shape. The hexagon could fit in a big pocket that would accept any shape, but the match would be less than optimal.



*Hall is head of the Laboratory of Structural Biology Macromolecular Structure Group. A 2D model of her human PUF RNA-binding domain appears on the monitor behind her in the photo. According to the JBC website, only the top one percent of papers submitted to the journal earn the honor of being selected as a paper of the week. (Photo courtesy of Steve McCaw)*



Hall explained what happens in the real world of cells this way. “RNA has four types of bases — adenine (A), uracil (U), guanine (G) and cytosine (C). In the PUF protein’s natural code, we could identify code sequences for, or sets of side chains that could recognize, A, U, and G, but nature didn’t show us a code for C. We weren’t completely thwarted by that, because one of the binding pockets could tolerate any base, and we could use this pocket for a single C and still design a specific RNA-binding protein. But, if we wanted to recognize an RNA sequence with more than one C, we were out of luck, and any protein that was designed to recognize a sequence containing one C would recognize not just one, but four related RNA sequences.”

With this thought in mind, Hall’s group successfully collaborated with the lab headed by [Zefeng Wang, Ph.D.](#), at the University of North Carolina at Chapel Hill, to use yeast to select a code for C, giving the ability to design a PUF domain that can recognize any RNA sequence. Now, researchers can design RNA-binding domains to recognize over 64,000 different sequences instead of roughly 9,000. To demonstrate the utility, they attached splicing machinery to a new RNA-binding domain using the C code to make artificial splicing factors.

*Citation:* [Dong S, Wang Y, Cassidy-Amstutz C, Lu G, Bigler R, Jezyk MR, Li C, Hall TM, Wang Z. 2011. Specific and modular binding code for cytosine recognition in Pumilio/FBF \(PUF\) RNA-binding domains. J Biol Chem 286\(30\):26732-26742.](#)

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## Splicing in the fight against cancer

Hall said the application of their findings could lead to viable cancer treatment options. Changing the RNA splice form changes the protein that is produced and can change its function. Scientists could use artificial splicing factors in cancer cells to force them toward apoptosis or cell death. In theory, if the splicing factor were expressed in tumor cells from a patient who is taking anti-cancer drugs, the malignant cells would experience a higher rate of cell death.

An artificial splicing factor could also be used to eliminate the lifeline of cancer cells. Large tumors need a blood supply to survive, so along with a regimen of pharmaceutical compounds that inhibits angiogenesis, or the ability to build the blood vessels, a splicing factor could prevent the formation of the proteins needed in the process.

According to Hall, designing a specific RNA-binding protein was tricky business before the discovery of PUF proteins’ RNA-binding properties. She was fortunate because nature made this particular family of RNA-binding proteins very amenable for single-stranded RNA sequence recognition. The first crystal structures revealed most of the code. With the help of yeast in the current study, the code is solved.

“In the past, we tried using computers to predict what side chains would be able to recognize a C,” Hall continued. “It was exciting to see the code on paper, but the crystal structure let us see how it actually worked in 3D.”

# Interns participate in a series of scientific presentations

By Eddy Ball and Josh Zeldin

An important component of the NIEHS Summer Internship Program (SIP) spanned June and July, as interns attended four scientific presentations to complement their bench training experience this summer. The series began with a presentation by Acting Scientific Director David Miller, Ph.D., June 16 ([see story](#)), continuing with talks by Principal Investigators Humphrey Yao, Ph.D., Laboratory of Reproductive and Developmental Toxicology; Stavros Garantziotis, M.D., Laboratory of Respiratory Biology; and Patricia Jensen, Ph.D., Laboratory of Neurobiology.

As she did last summer, SIP Coordinator Debbie Wilson drew heavily on resources provided by NIEHS postdoctoral fellows and laboratory staff, who gave presentations, led group activities, and helped the featured speakers with hands-on activities. Attendance was excellent, with each of the presentations attracting a full audience of young people eager to learn more about the science conducted by investigators across several laboratories at NIEHS.

The talks were also webcast to trainees at NIH.

## Reproductive biology

[Yao](#), a developmental biologist who heads the NIEHS Reproductive Developmental Biology Group, focused his June 30 presentation on embryo development and sexual differentiation, abnormalities of which are linked to birth defects, such as ambiguous genitalia and pseudohermaphroditism, and conditions with a fetal origin that develop in adulthood. “Birth defects in reproductive organs are rarely fatal,” Yao explained, “but may result in fertility problems and abnormal growth in tissue that could lead to tumor formation when individuals reach adulthood.”

Ambiguous external genitalia occurs roughly in 1 of 2000 births, Yao said, and infertility is an increasingly common public health issue. The financial burden of treating infertility is significant, but there is no accurate way to estimate the social and emotional implications of health problems caused by abnormalities in embryo development.

Following Yao’s introduction, postdoctoral fellows Valerie Davis, Ph.D., Nisha Cavanaugh, Ph.D., and Tracy Clement, Ph.D., took the podium and provided more details on the reproductive system and examples of what research on reproductive biology is conducted at NIEHS. The presentation ended with an informal



*Yao was obviously more comfortable moving around and working the crowd, often with humor and direct engagement. Three of his postdoctoral assistants laughed along with trainees, as Yao laced his science with wit and charm. (Photo courtesy of Steve McCaw)*



*Postdoctoral fellow Valerie Davis, Ph.D., has participated in a number of outreach workshops this year, and she’s developing an engaging teaching style of her own. (Photo courtesy of Steve McCaw)*



exercise to get interns involved in designing an experiment to answer a typical research question, whether maternal exposure to a certain chemical affects testes development of the offspring.

When interns had correctly identified the seven things an investigator needs to consider, postdoctoral fellows Sarah Swerdlow, Ph.D., and Staton Wade, Ph.D., opened up the auditorium to a bank of microscopes with slides showing sperm mobility and mouse embryos. Yao and his assistants helped interns understand what they were seeing.

## Respiratory biology

[Garantziotis](#), a pulmonologist who heads the NIEHS Matrix Biology Group and also serves as medical director of the NIEHS Clinical Research Unit, gave a presentation July 7 that offered both a sweeping overview of the lung and a fantastic voyage through its progressively smaller and more numerous passageways. He revealed his bias early in his talk, when he said, “The lung is the coolest organ in the body.” To back up that statement, he wowed his audience with the sheer volume of the lung — its 300 million alveoli and its total surface area of 450-900 square feet — as well its daily ventilation of approximately 10,000 liters of air each day per day at rest, as it filters some 10,000 liters of blood.

The lung’s vulnerability to inhaled particles as large as one millimeter in diameter to ones smaller than 10 micrometers led naturally into a discussion of environmental airway disease, such as asthma and chronic obstructive pulmonary diseases (COPD). Garantziotis emphasized the public health implications of lung disease, noting COPD, the fourth most common cause of death worldwide, costs \$40 billion annually in the U.S. alone. In developed countries, the leading cause of COPD is lifestyle, primarily smoking, but in the developing world, the main cause is indoor cooking with biomass.



*Intern Sabrina Murray, a veterinary student, looked right at home at the microscope. For some of the younger interns, this was one of the first times they’ve used scopes with this degree of magnification. (Photo courtesy of Steve McCaw)*



*Garantziotis underscored nature’s elegant design when he told the interns that artificial lungs work only for a couple of days at best. (Photo courtesy of Steve McCaw)*



*Back for his second year as an intern, Zack McCaw, center, looks as though Garantziotis’ enthusiasm was contagious. McCaw is all eyes and ears as he joined Garantziotis on the fantastic voyage through the lung. (Photo courtesy of Steve McCaw)*

NIEHS Biologist Michelle Sever followed Garantziotis with a discussion of her doctoral thesis on the association between indoor air pollution and stress related to community violence, on the one hand, and asthma among inner city children, on the other.

## Neurobiology

[Jensen](#), a neuroscientist who heads the Developmental Neurobiology Group, wrapped up the series with her presentation on the environment and the developing brain July 14. Like Garantziotis, she impressed interns with the size of what she described as “the most complex organ in the body [that] controls all of our senses, our actions, perceptions, and thoughts.” She described the brain’s approximately 100 billion neurons and 60 trillion synapses that occupy a three-pound structure about the size of a grapefruit. She used the visual image of the 1.4 billion acre Amazon rain forest, comparing the number of neurons to the number of trees there, and the number of synapses to the number of leaves on those trees.

Emphasizing the vulnerability of the brain, Jensen told the audience that it begins developing three weeks into gestation and isn’t fully developed until late adolescence. Over this period of time, she said, there are critical periods when the brain is especially vulnerable to environmental insult from exposure to heavy metals, smoke, pesticides, and other compounds. Diseases that may be caused or aggravated by environmental exposures, such as autism spectrum disorders and Parkinson’s, Jensen added, create a heavy public burden in terms of treatment costs and loss of productivity.

Jensen spoke briefly of the interplay of epidemiological, behavioral, and cellular and molecular studies in neurobiological research, as well as her current project involving genetic fate mapping of molecularly defined subdomains within the noradrenergic primordium. Interns spent the last half of the presentation period touring the five labs that make up the Laboratory of Neurobiology, and interacting with postdoctoral fellows who discussed ongoing projects in their respective groups.

(Josh Zeldin is a summer intern with the NIEHS Office of Communications and Public Liaison. He is a student at the University of North Carolina at Chapel Hill.)

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*Sever developed her interest in indoor air pollution during her work as a biologist in the Laboratory of Respiratory Biology and decided to pursue a doctorate in epidemiology. She traced her interest in environmental health back to her own experiences as a summer intern at NIEHS. (Photo courtesy of Steve McCaw)*



*Jensen, shown in her lab, said she wants to understand how the diversity in brain neurons comes about and how subpopulations of cells in the brain differ from one another. She said that during critical periods of development, environmental exposures can influence the making and pruning of synapses in the brain. (Photo courtesy of Steve McCaw)*



# Committee recommends alternative method for product safety testing

By NICEATM

In July, recommendations from the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) were transmitted to federal agencies for using alternative method safety testing results to identify substances that have a high potential for causing allergic contact dermatitis (ACD) in humans.

NIEHS/NTP Director Linda Birnbaum, Ph.D., forwarded the ICCVAM recommendations on behalf of the Secretary of Health and Human Services. ICCVAM, an interagency committee of the U.S. federal government, is administered by the National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), a center within the NTP at NIEHS.

NICEATM provided scientific support to the ICCVAM interagency working group that developed the recommendations (see text box).

## Murine local lymph node assay

According to the U.S. Bureau of Labor Statistics, occupational skin diseases are the most common type of occupational illness. Many of these cases arise from exposure to skin-sensitizing substances, which can lead to the development of ACD.

ACD is a delayed hypersensitivity reaction caused by an immune response after repeated exposures to a skin-sensitizing substance. People with ACD typically experience redness, itching, swelling, or blistering of the skin after re-exposure to the sensitizing substance. Studies have shown that ACD has a significant adverse impact on quality of life in affected individuals.

The recent ICCVAM recommendations are for use of the murine local lymph node assay, or LLNA, to categorize the potency of chemicals that cause ACD in humans. ICCVAM concluded that the LLNA can be used to categorize some substances as strong skin sensitizers. Strong skin sensitizers are those substances considered to have a high potential for causing ACD in humans.

The LLNA uses fewer animals than other commonly used test methods for ACD hazard determination that use guinea pigs. The LLNA also eliminates the discomfort that can be experienced by animals when the guinea pig test methods are used. Other advantages of the LLNA are that it can be performed more rapidly and it provides dose-response information.



*The current ICCVAM recommendations were finalized after considering comments from an international independent peer review panel. Here, NICEATM Director William Stokes, D.V.M., center, appears with two members of the panel at their meeting at CPSC headquarters. Pictured with Stokes are Dagmar Jirová, M.D., Ph.D., left, toxicologist at the National Institute of Public Health, Czech Republic, and Nathalie Alépée, Ph.D., right, research manager at L'Oréal Research and Development in France. (Photo courtesy of NICEATM)*

## ICCVAM interagency Immunotoxicity Working Group

The ICCVAM interagency Immunotoxicity Working Group (IWG) developed the recommendations with support from NICEATM. The IWG is co-chaired by Abigail Jacobs, Ph.D., of the U.S. Food and Drug Administration (FDA) and Joanna Matheson, Ph.D., of the CPSC. It includes scientists from the CPSC, Environmental Protection Agency, FDA, NIEHS, and the National Institute for Occupational Safety and Health. NIEHS scientists Dori Germolec, Ph.D., William Stokes, D.V.M., and Warren Casey, Ph.D., contributed to the ICCVAM recommendations. Stokes is director of NICEATM and executive director of ICCVAM.

For more than 10 years, the LLNA has been accepted worldwide as a valid alternative to guinea pig methods for identifying chemicals with the potential to cause ACD. However, the use of the LLNA has been limited to a yes/no determination of whether or not a substance has the potential to cause ACD in humans. Availability of a test method that could be used to identify substances as strong human skin sensitizers would be helpful to regulatory agencies such as the U.S. Consumer Product Safety Commission (CPSC).

### Categorizing potentially hazardous substances

The Globally Harmonized System of Classification and Labeling of Chemicals, or GHS, is a hazard classification system developed by the United Nations for use by governments to inform workers and consumers of potential hazards. The ICCVAM evaluation assessed the extent to which a GHS criterion based on LLNA results can correctly categorize substances as strong sensitizers, Subcategory 1A, and determined that the GHS criterion correctly identifies about half of known human strong skin sensitizers. ICCVAM concluded that additional information would need to be considered to confirm whether substances that do not meet this criterion are or are not strong sensitizers

The ICCVAM test method evaluation report, which contains the complete ICCVAM recommendations, is available on the NICEATM-ICCVAM [website](#). The current recommendations complete a series of evaluations that NICEATM and ICCVAM have been conducting on the LLNA. Other ICCVAM recommendations to Federal agencies on new versions and applications of the LLNA can also be found on the NICEATM-ICCVAM [website](#).



*This collage of pictures representing the use of the murine LLNA for potency categorization of chemicals causing allergic contact dermatitis in humans includes, clockwise from top left, scintillation vials used to measure the quantity of radioactive tracer chemical incorporated into dividing lymph node cells; flasks and bottles containing liquids representing chemicals; a human clinical patch test for skin allergy; a graph of data used in the evaluation of the murine LLNA for potency categorization; and a lab technician resuspending cells in a plastic tube. (Graphic courtesy of NICEATM)*

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# This month in EHP

By Eddy Ball

The cover of the August issue of [Environmental Health Perspectives \(EHP\)](#) blends a colorful abstract human image with machinery and geometric shapes to underscore the title of its feature news story, “A Study in Balance: How Microbiomes Are Changing the Shape of Environmental Health.” As appreciation of the communities of bacteria that inhabit the human body grows among the scientific community, investigators are exploring how microbiomes might serve as intermediaries in the process of environmental exposure and affect host susceptibility.

A second news story addresses an issue more and more states are facing — proposals to extract shale gas by a process known as hydraulic fracturing, or fracking. “Blind Rush? Shale Gas Boom Proceeds amid Human Health Questions” discusses what we know about fracking, and what research still needs to be done to answer lingering questions about potential human health effects and ecologic problems associated with the procedure.

In this month’s [Researcher’s Perspective](#) podcast, author [Luz Claudio, Ph.D.](#), revisits her influential 2007 EHP news feature article, “[Waste Couture: Environmental Impact of the Clothing Industry.](#)” In a conversation with host Ashley Ahearn, Claudio discusses her inspiration for the story and why it has captured so much attention.

Featured commentary, reviews, and research this month includes the following:

- MeHg and Plasma Paraoxonase Activity
- Diabetes, Arsenic, and High-Fat Diet
- Canadian National Air Pollution Models
- Engine Operating Conditions and Exhaust Toxicity
- Mammary Gland Development
- Organophosphates and Child Neurodevelopment

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# Extramural papers of the month

*By Author*

- [Some BPA-free bottles live up to their claim](#)
- [Genetic link determined for prostate cancer in African-American men](#)
- [Caffeine and UVB damage](#)
- [Prostate cancer risk increased with ambient exposure to pesticides](#)



Read the current Superfund Research Program [Research Brief](#). New issues are published on the first Wednesday of each month.

## Some BPA-free bottles live up to their claim

University of Cincinnati researchers tested a variety of bottles claiming to be bisphenol A free and found some conflicting results, according to a new study. The NIEHS-funded study was prompted by consumer concerns and was conducted to see if bottles made of materials other than polycarbonate lived up to their claim or leached BPA into water stored in them for five days.

The bottles tested were obtained from retail sources and were made of polycarbonate, stainless steel, copolyester, aluminum with a copolyester lining, or aluminum with an epoxy resin lining.

As expected, the lab found that water stored in polycarbonate bottles contained BPA at the end of the five days. This confirmed previous results from the same lab. Aluminum bottles coated with an epoxy resin gave conflicting results depending on the manufacturer. Bottles obtained from discount stores released significantly more BPA.

The researchers conclude that just because a bottle is not made of polycarbonate, it is not necessarily free of BPA. Some alternative bottles were indeed BPA free but, based on these findings, consumers should be wary.

*Citation:* [Cooper JE, Kendig EL, Belcher SM](#). 2011. Assessment of bisphenol A released from reusable plastic, aluminum and stainless steel water bottles. *Chemosphere*; doi:[10.1016/j.chemosphere.2011.06.060](#) [Online 7 July 2011].

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## Genetic link determined for prostate cancer in African-American men

Scientists at the Keck School of Medicine of the University of Southern California have found a single-nucleotide polymorphism that occurs in about five per cent of African-American men, putting them at greater risk for developing prostate cancer. This research was supported by NIEHS and the National Cancer Institute.

The study examined about one million single-nucleotide polymorphisms across the genomes of 3,425 African-American men with prostate cancer and 3,290 African-American controls. The study is part of the Multiethnic Cohort study being conducted in a collaborative effort between the Keck School and the University of Hawaii.



In general, men of African descent are more susceptible to prostate cancer than others. The current study reports the discovery of a prostate cancer marker on chromosome 17 and builds on a previous finding by the same research team that elucidated a marker on chromosome 8. These studies support the need for additional genome-wide association studies to locate markers that may play a role in understanding racial and ethnic health disparities.

*Citation:* [Haiman CA, Chen GK, Blot WJ, Strom SS, Berndt SI, Kittles RA, Rybicki BA, Isaacs WB, Ingles SA, Stanford JL, Diver WR, Witte JS, Hsing AW, Nemesure B, Rebbeck TR, Cooney KA, Xu J, Kibel AS, Hu JJ, John EM, Gueye SM, Watya S, Signorello LB, Hayes RB, Wang Z, Yeboah E, Tettey Y, Cai Q, Kolb S, Ostrander EA, Zeigler-Johnson C, Yamamura Y, Neslund-Dudas C, Haslag-Minoff J, Wu W, Thomas V, Allen GO, Murphy A, Chang BL, Zheng SL, Leske MC, Wu SY, Ray AM, Hennis AJ, Thun MJ, Carpten J, Casey G, Carter EN, Duarte ER, Xia LY, Sheng X, Wan P, Pooler LC, Cheng I, Monroe KR, Schumacher F, Le Marchand L, Kolonel LN, Chanock SJ, Berg DV, Stram DO, Henderson BE. 2011. Genome-wide association study of prostate cancer in men of African ancestry identifies a susceptibility locus at 17q21. Nat Genet 43\(6\):570-573.](#)

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## Caffeine and UVB damage

According to recent findings from a team led by an NIEHS grantee at the University of Chicago, Outstanding New Environmental Scientist (ONES) awardee and former NIEHS fellow Yu-Ying He, Ph.D., caffeine promotes UVB-induced apoptosis, or programmed cell death, of unrepaired keratinocytes, thereby preventing carcinogenic transformation of the cells. Caffeine produces complex pharmacological actions and has been shown to be chemopreventive in non-melanoma skin cancer in humans and in mice.

These researchers investigated the molecular and cellular mechanisms involved in the pro-apoptotic effect of caffeine on UVB-irradiated HaCaT keratinocytes. Keratinocytes are the predominant cell type in the outermost layer of the skin. Pretreatment with caffeine increased UVB-induced apoptosis in the cultured keratinocytes. The experiments also showed that caffeine mediated to critical oncogenic pathways in skin tumorigenesis.

These findings build on previous work that demonstrated that coffee and regular exercise work together to kill off precancerous cells whose DNA has been damaged by UVB radiation.

*Citation:* [Han W, Ming M, He YY. 2011. Caffeine Promotes Ultraviolet B-induced Apoptosis in Human Keratinocytes without Complete DNA Repair. J Biol Chem 286\(26\):22825-22832.](#)

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## Prostate cancer risk increased with ambient exposure to pesticides

A new study from NIEHS-supported epidemiologists at the University of Southern California found that exposure to certain agricultural pesticides increases the risk of prostate cancer. This study adds to the mounting research that suggests insecticides, fungicides, and herbicides wreak havoc on the male endocrine system.

Exposure to methyl bromide and other organochlorine pesticides was associated with an up to two-fold increase in prostate cancer risk in the 173 men with prostate cancer in the study, when compared to controls. Captain,

a fungicide used widely on apple orchards in the U.S., was associated with prostate cancer as well, but only at relatively high levels of exposure. The researchers conclude that efforts to limit the spread of pesticide residues into the environment are not as protective as they need to be to limit human exposure.

According to the study, the most likely reason for the increased risk is a complex interplay of genetics and the environment. The researchers speculate that only those men with a certain genotype will develop prostate cancer if they are exposed to pesticides. Preventing exposure by reducing the use of pesticides, increasing organic growing practices, and other methods of limiting contact with pesticides would most likely prevent the disease from developing or progressing in these susceptible populations.

*Citation: Cockburn M, Mills P, Zhang X, Zadnick J, Goldberg D, Ritz B. 2011. Prostate cancer and ambient pesticide exposure in agriculturally intensive areas in California. Am J Epidemiol 173(11):1280-1288.*

(Jerry Phelps is a program analyst in the NIEHS Division of Extramural Research and Training.)

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## Intramural papers of the month

*By Raluca Dumitru, Ian Thomas, Darshini Trivedi, and Angelika Zaremba*

- [The importance of mechanical stretch in lung epithelial injury](#)
- [NIEHS study investigates the impact of poised RNA polymerase II on neuronal gene transcription](#)
- [Expanded DNA methylation analysis reveals new functional sequences of the genome](#)
- [The regulation of survivin expression in UVB-exposed mouse skin](#)

## The importance of mechanical stretch in lung epithelial injury

Investigators from NIEHS and Duke University have uncovered the mechanism by which the mechanical stretch of the lung epithelia can lead to lung scarring. Mechanical stretch usually occurs during mechanical ventilation of patients with acute or chronic lung conditions. This study is the first to demonstrate that stretch injury of the alveolar epithelia can induce epithelial to mesenchymal transition (EMT), responsible for scarring, via the activation of innate immunity.

Researchers used cells that line the deepest part of the lung, called alveolar type II cells (AT2) isolated from mice and subjected them to mechanical stretch. These *in vitro* experiments first confirmed that mechanical stretch induces EMT, which means that cells change their appearance and behavior from epithelial (surface lining cells) to mesenchymal (scar cells). This was confirmed by a decrease of the epithelial marker E-cadherin and an increase in the mesenchymal markers vimentin and alpha-smooth muscle actin.

Further, stretch-induced EMT was shown to involve the innate immune system because mechanical stretch was not able to induce EMT in AT2 cells from mice deficient in the innate immune adaptor MyD88. Lastly, researchers found that mechanical stretch in the AT2 cells activates the Wnt/beta-catenin pathway by examining a number of genes from that pathway including *wisp1*.



While *in vivo* studies are recommended, this work represents an important step toward understanding the molecular mechanisms underlying ventilator induced epithelial injury.

*Citation:* [Heise RL, Stober V, Cheluvvaraju C, Hollingsworth JW, Garantziotis S.](#) 2011. Mechanical stretch induces epithelial-mesenchymal transition in alveolar epithelia via hyaluronan activation of innate immunity. *J Biol Chem* 286(20):17435-17444.

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## **NIEHS study investigates the impact of poised RNA polymerase II on neuronal gene transcription**

In a recent study examining the transcription of immediate early genes (IEGs) in neurons, NIEHS scientists found strong evidence that the rapid induction of neuronal IEGs requires poised RNA polymerase II (Pol II), thus suggesting a role for this mechanism in a wide range of processes including learning and memory.

Three observations were made to support the role of Pol II stalling in neural activity-induced rapid transcription. The first finding made use of genome-wide sequencing to find that this particular enzyme is enriched in the proximity of Arc promoters and those of all other IEGs with similar response kinetics. Secondly, with the introduction of negative elongation factor RNA interference (NELF RNAi), the researchers found that the rapid kinetics of all such rapid IEGs are dependent on Pol II stalling. Finally, IEGs with slower responses were found to lack Pol II stalling in most instances and, as such, they remained unaffected by NELF RNAi.

Ultimately, the data derived from this study support the idea that rapidly induced IEGs are a specialized subset of genes poised for an immediate response mediated by Pol II stalling, though investigators are quick to note that further testing is required to determine the role of this process in brain function and behavior.

*Citation:* [Saha RN, Wissink EM, Bailey ER, Zhao M, Fargo DC, Hwang JY, Daigle KR, Fenn JD, Adelman K, Dudek SM.](#) 2011. Rapid activity-induced transcription of Arc and other IEGs relies on poised RNA polymerase II. *Nat Neurosci* 14(7):848-856.

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## **Expanded DNA methylation analysis reveals new functional sequences of the genome**

NIEHS researchers and scientists from the Johns Hopkins University in Baltimore designed a new method to identify targets of methylation-mediated epigenetic processes throughout the genome and revealed a large unexpected number of non-CpG island (CGI) unmethylated genomic regions (UMRs) with the highest enrichment in regulatory elements.

DNA methylation is a widespread modification in the vertebrate genome. This epigenetic modification of the DNA influences human development and disease. The scientists developed a high-throughput sequencing-based DNA methylation analysis, by expanding the version of the methyl-sensitive cut counting assay (MSCC).

DNA methyltransferases primarily target the cytosines located at CpG dinucleotides for chemical modification. MSCC addresses only CpGs in the context of the CCGG site, leaving out the possible 16 XCGX tetranucleotide combinations in which CpGs are found. By including three additional enzymes the researchers expanded MSCC to address a total of 5 of the 16 XCGC combinations, sampling 30 percent of CpG at genome wide and 50 percent of those located at CpG islands.

Applied to mouse liver DNA, they confirmed reported data showing hypomethylations concentrated at promoters and in CGIs. However 50 percent of the detectable unmethylated regions do not overlap algorithm-defined CGIs and offer a novel search space to screen for functionally relevant epigenetic loci in development and disease.

*Citation:* [Colaneri A, Staffa N, Fargo DC, Gao Y, Wang T, Peddada SD, Birnbaumer L](#). 2011. Expanded methyl-sensitive cut counting reveals hypomethylation as an epigenetic state that highlights functional sequences of the genome. *Proc Natl Acad Sci U S A* 108(23):9715-9720.

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## The regulation of survivin expression in UVB-exposed mouse skin

A recent study by NIEHS investigators examined a novel mechanism by which the prostaglandin (PG) E2 receptor, EP2 protects against ultraviolet (UV)-induced apoptosis in mouse skin. In the current study, the investigators examined the induction of survivin, a member of the inhibitor of apoptosis family, as an additional mechanism by which the inflammatory enzyme cyclooxygenase-2 (COX-2) and PGE<sub>2</sub> mediate anti-apoptotic effects.

Previous work by this group has shown that COX-2 induction and the stimulation of EP2/EP4 by PGE<sub>2</sub>, protects against UVB-induced epidermal apoptosis by activating the anti-apoptotic protein p-Bad. PGE<sub>2</sub>, the primary PG produced following UV exposure, mediates its biological activities by binding to four different receptors, EP1, EP2, EP4 and EP4.

Genetic or pharmacological inactivation of COX-2 reduced UVB-induced survivin expression and treatment with an EP2-specific agonist partially restored survivin levels. To determine the mechanism by which EP2 was involved in inducing survivin expression, the role for the pSTAT3, a transcription factor known to regulate survivin levels, as well as the epidermal growth factor receptor (EGFR), a downstream effector of EP2, was investigated.

The results show that COX-2 derived PGE<sub>2</sub> regulates survivin expression by activating EP2 and the resultant transactivation of EGFR and STAT3. These studies suggest the EP2/survivin pathway is a potential target for skin cancer therapy.

*Citation:* [Chun KS, Langenbach R](#). 2011. The prostaglandin E2 receptor, EP2, regulates surviving expression via an EGFR/STAT3 pathway in UVB-exposed mouse skin. *Mol Carcinog* 50(6):439-448.

(Raluca Dumitru, M.D., Ph.D., is an Intramural Research Training Award fellow in the Cell Biology Group of the Laboratory of Molecular Carcinogenesis. Ian Thomas is a writer/editor in the NIEHS Office of Communications and Public Liaison. Darshini Trivedi, Ph.D., is a postdoctoral fellow in the NIEHS Metabolism and Molecular Mechanisms Group of the Laboratory of Toxicology and Pharmacology. Angelika Zaremba, Ph.D., is a visiting postdoctoral fellow in the NIEHS Laboratory of Signal Transduction Inositol Signaling Group.)

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# Inside the Institute

## Feds Feed Families off to a great start at NIEHS

By Eddy Ball


If the first two drop-box collections June 28-30 and July 27 are any indication, NIEHS is poised to set new records for food donations in 2011. Still, the Institute's **Feds Feed Families (FFF)** organizers say the need is so great ([see text box](#) for what's accepted) that they're calling for more volunteers — and more donations — to help this year's drive set a new standard for philanthropy at NIEHS.



**Linked video:**  
[OPM Director challenges federal employees to beat 1.7 million pounds of non-perishables collected last year \(02:06\)](#)

John Berry

(Launches in new window)

Download Media Player:  Flash 

The first delivery June 30 weighed in at more than 500 pounds, equivalent to almost half of the entire amount collected in 2010. Food collected during the July 27 pickup added 740 pounds, driving the mid-drive total to 1,240 pounds. Organizers are striving to beat that total substantially with the next collection August 31 from 7:30-9:00 a.m.

NIEHS/NTP Director Linda Birnbaum, Ph.D., says she hopes to get the kind of support for FFF that the Combined Federal Campaign has enjoyed for years. In her message to employees, Birnbaum pointed to high unemployment and the drain food banks nationwide are experiencing, as well as the big difference employees could make. "This is a great way for NIEHS to show our concern for the well-being of our neighbors in the North Carolina community," she wrote.

As it was last year, the drive at NIEHS is organized and sponsored by the American Federation of Government Employees (AFGE) 2923, Blacks In Government (BIG), and the NIEHS Office of Management (OM), to collect food for delivery to the [Durham Rescue Mission](#) and the [Food Bank of Central and Eastern North Carolina](#).

### Efforts nearly double in 2011

At the national level, FFF organizers were so impressed with the level of donations in 2010 that they raised their goals almost 100 percent,



Organizers gathered with some of the food and hygiene items from the first collection June 28. Shown, left to right, are Wells, Rice, and Jirles. (Photo courtesy of Steve McCaw)



from 1.2 million pounds of non-perishable food and other items to 2 million pounds across the federal workforce. Last year NIEHS employees contributed 1,051 pounds out of a total NIH contribution of 13,000 pounds.

This year the U.S. Department of Health and Human Services has upped its goal to 83,300 pounds and, in a recent message to everyone at NIH, Director Francis Collins, M.D., Ph.D., offered this proposal: “This year, let’s set a goal of every NIH employee donating five pounds of non-perishable food, which is enough to feed one family one meal.” Some federal agencies are issuing public challenges to their colleagues at other agencies, in a spirit of good-natured philanthropic competition.

### Getting involved

Becoming a part of FFF is as easy as an email or phone call to the organizers — AFGE coordinator [Bill Jirles](#) at 919-541-2637, BIG coordinator [Annette Rice](#) at 919-541-4410, or NIEHS OM coordinator [Monya Wells](#) at 919-541-1952. Drop boxes are conveniently located throughout the main campus and in the Keystone Building.

### Building a village of volunteers

The number of volunteers from across NIEHS/NTP grows by the week. Early joiners include William Boyd, Juanita Bradley, Sally Fields, Margaret George, Veronica Godfrey Robinson, Dianne Gray, Judy Hanson, Chris Long, Dennis Malone, Jackie Osgood, Michelle, Owens, Dudley Riner, VeeVee Shropshire, Mike Tyson, Mitzie Walker, Myra Westmoreland, and Sheila Withers. If the level of donations is as great as organizers anticipate, FFF will need even more volunteers to handle drop-box distribution and the final collection on August 31.

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## Future scientists are exposed to everyday chemistry

*By Melissa Kerr*

Many NIEHS scientists and staff members volunteered their time and expertise to show the youth of the area that chemistry is everywhere during a science education program June 25 in Durham, N.C., as the [Durham Alumnae Chapter of Delta Sigma Theta Sorority Science](#) and Everyday Experiences (SEE) program held its sixth annual day camp with the theme “Celebrating the Year of Chemistry.”

Around 40 children, ages 9 through 14, from Durham and surrounding areas, participated in the half-day

### Most needed items for 2011 Feds Feed Families

FFF cannot accept any glass containers. Please donate the following kinds of items in paper, plastic, metal, or cloth containers:

- Canned meals, seafood, and meats
- Canned fruits and vegetables
- Cereal
- Peanut butter
- Rice, pasta, and dried beans
- Infant products
- Hygiene items



*Beard, center, welcomed the young group to the 6th annual SEE Camp at Delta House in Durham. (Photo courtesy of Melissa Kerr)*



program at the Delta House. The camp was designed to provide the campers and several of their parents an opportunity to view the wonders of the mundane through the lens of chemistry.

Durham SEE chair Sharon Beard, an industrial hygienist with the NIEHS Worker Education and Training Program, said her focus is outreach. Scientists were invited not only from NIEHS, but also from North Carolina Central University (NCCU), North Carolina State University (NCSSU), Duke University, and the N.C. Chapter of the American Chemical Society. “One of our goals is to get chemists into the community,” Beard explained.

The day began with a morning workout for the children, parents, and volunteers. Not only were the children provided with balls, hula hoops, and jump ropes, the volunteers also led a group dance. After a welcome from Beard, the participants separated into three groups with the parents forming one of their own (see text box).

### A full program of hands-on learning

NIEHS scientists Elena Braithwaite, Ph.D., a staff scientist in the Comparative Genomics Group, and Danielle Watt, Ph.D., a postdoctoral fellow in the DNA Replication Fidelity Group, ran a program designed to teach young children the basics of polymers, acids, and bases. The children used balloons and petroleum jelly to learn about air pressure. Braithwaite and Watt also brought out several everyday chemicals to illustrate their practical applications.

Watt, in her third year of volunteering with the SEE camp, believes the children should learn that chemistry does not stop at the classroom door. She said, “I feel if we can relate science to something [the children] do every day, they wouldn’t shy away from it so much.”

Darlene Taylor, Ph.D., and Tonya Gerald, Ph.D., professors at NCCU, taught the older campers as they tried their hands at making two different polymers, Obleck and Goop. The participants in this group also ran some experiments examining the chemical properties of cooked cabbage using acids and bases.

Taylor explained that it is important for young people to have hands-on and fun exposure to science. “SEE Camp is particularly important because of the diverse [educational backgrounds of] students who participate in this camp. Diversity is a key element in creativity,” she explained.



*The participants were encouraged to get the blood pumping during a morning workout. (Photo courtesy of Melissa Kerr)*



*The campers get ready for hands-on, everyday science. (Photo courtesy of Melissa Kerr)*



*One of the campers’ parents assisted a group to successfully impale a balloon with a wooden skewer. (Photo courtesy of Melissa Kerr)*

William Switzer, Ph.D., from NCSU, taught the younger students about the states of matter. He demonstrated several ways that matter can maintain its state, as well as how it can be manipulated in unique ways, including the ever-popular use of dry ice. Switzer said he hopes to instill an interest in chemistry, and science in general, into the youth of local communities. “It’s incredibly important for young people to maintain interest in the sciences,” he explained.

### **Making science a family affair**

Many of the camp activities were set up specifically so that parents could participate and perhaps extend the learning into the child’s everyday life. Rhonda Powell, mother of 8-year-old twins from Raleigh, was excited to have her children participate in the SEE camp. “I think if you can do math and science, you can do anything,” she said.

The SEE initiative of Delta Sigma Theta Sorority encourages African-American children to continue to show interest in science and mathematics through immersion in fun, thought-provoking activities that can translate into everyday life. The program strives to make science education a family affair by reaching out to children and their parents.

(Melissa Kerr studies chemistry at North Carolina Central University. She is currently an intern in the NIEHS Office of Communications and Public Liaison.)



*Watt, right, explained acid and base properties to a group of young campers. (Photo courtesy of Melissa Kerr)*



*Gerald, standing, led a group of young scientists in pipetting acid for an experiment. (Photo courtesy of Melissa Kerr)*

## **Involving parents in science education**

Marian Johnson-Thompson, Ph.D., professor emerita of biology and environmental science at the University of the District of Columbia and retired NIEHS director of Education and Biomedical Research Development, and Joan Packerham, Ph.D., director of the NIEHS Office of Human Research Compliance, led a session for parents. Parents learned about programs specifically designed to expand a youth’s interest in science and math. In addition, parents picked up many ideas for incorporating scientific and mathematic principles into their everyday home activities, through grocery shopping, cooking, gardening, composting, cleaning, and outdoor activities.

An example that parents found interesting was capturing fireflies, or lightning bugs, watching them luminesce, and then talking about the chemical mechanism of bioluminescence. Parents were told not to shy away from exploring science because they may not be familiar with the scientific and mathematical principles themselves, but to use the experience as an opportunity to explore and learn with their children. Their instructors reminded parents that the internet could provide all the information they would need.





*Switzer, left, discussed states of matter with a young camper.  
(Photo courtesy of Melissa Kerr)*



*Packenhams, right, and Johnson-Thompson, center, explored opportunities that parents can provide for their children.  
(Photo courtesy of Melissa Kerr)*



*NIEHS staff and scientists took an opportunity to help the local community. Shown, left to right, are Martha Barnes, program analyst with the Program Analysis Branch, Johnson-Thompson, Beard, Watt, Packenhams, and Braithwaite. Not Pictured: Shawn Jeter, a technical information specialist in the Information and Data Management Workgroup. (Photo courtesy of Melissa Kerr)*

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# NIEHS and NIH personnel unite for disabilities awareness

By Ian Thomas

According to the latest statistics released in June by the U.S. Department of Labor, the unemployment rate among Americans with disabilities soared nearly 8 percent higher than the 9 percent national average. For that reason, NIH officials hosted an innovative new seminar June 22 at NIEHS designed to promote disabilities awareness.

Conducted by the NIH Office of Equal Opportunity and Diversity Management (OEODM), the session sought to highlight many of the Federal employment incentives available to people with disabilities, while also seeking to dispel many of the myths surrounding their role in the workplace.

“More times than not, people meet the disability before they meet the person,” explained Gerard Roman, an equal employment opportunity (EEO) specialist with OEODM based at NIEHS. “Disabilities don’t discriminate and it’s important for people to know that individuals with a disability may be able to perform the essential functions of a job, with or without an accommodation.”

Over the span of two hours, seminar participants discussed a wide variety of topics, ranging from Federal laws such as the [Americans with Disabilities Act \(ADA\)](#) as amended, to the responsibilities of organizations such as NIEHS, before concluding with a step-by-step breakdown of the reasonable accommodations process itself — something many deem critical to the quest for equality.

“Reasonable accommodations are all about communication,” explained Kimberly Kirkpatrick, the disability employment program manager with NIH and the seminar’s instructor. “If today’s attendees take nothing else away from this class, I hope they understand that accommodating individuals with disabilities should be a simple, interactive process between the employee and the supervisor. The ADA Amendments Act clarifies that it is not intended to be a complicated process.”

Kirkpatrick and others agreed that while education seminars like this, in concert with ambitious new initiatives like the [Schedule A Hiring Authority](#), the [Computer/Electronics Accommodations Program \(CAP\)](#), and the [Job Accommodation Network \(JAN\)](#), are impressive steps toward equality, the climb is far from over. To that end, the U.S. Department of Health and Human Services has taken steps to raise the bar with its ambitious goal to have 2.5 percent of its total workforce comprised of individuals with severe or targeted disabilities by 2016.



*Kirkpatrick said that the ADA Amendments Act of 2008 shifts the focus from the disability to responsibility of employers for providing the most effective reasonable accommodation. (Photo courtesy of Jennifer Weinberg)*



*Event host Roman is striving to make sure NIEHS employees have opportunities to learn about their rights and obligations when it comes to accommodation. He gave a presentation himself in March 2009 ([see story](#)) about the ADA Amendments Act of 2008. (Photo courtesy of Jennifer Weinberg)*



“Moving forward, we have to get employees over their fear of requesting accommodations and we have to get supervisors over their fear of having open and honest discussions with their employees, disabled or not,” said Kirkpatrick. “In terms of awareness, we’ve got to be more proactive in getting the word out to the general public. The government has a lot of exciting opportunities open to people with disabilities and, at the end of the day, it’s up to us to let them know that we genuinely want them to work for us.”

(Ian Thomas is a writer/editor in the NIEHS Office of Communications and Public Liaison)



*Participants represented virtually every division of NIEHS. Administrative Specialist Pinkney Wilder, above, for example, works in the Division of Intramural Research Laboratory of Signal Transduction. (Photo courtesy of Jennifer Weinberg)*



*Because her job impacts accommodation so directly, NIEHS Office of Management Interior Designer Amanda Thompson benefited greatly from Kirkpatrick’s talk and the resources she described. (Photo courtesy of Jennifer Weinberg)*



*NIH Electrical Engineer Sam Musulin works for the Facilities Operations Branch overseeing property at NIEHS. He was one of several members of his team at the workshop. (Photo courtesy of Jennifer Weinberg)*



*NTP Cellular and Molecular Pathology Branch (CMPB) Biologist Tina Jones, center, who is currently co-chair of the Disability Advocacy Committee, was on hand along with CMPB colleague Biologist Julie Foley, not shown. (Photo courtesy of Jennifer Weinberg)*

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# Students from Duke summer program tour NIEHS

*By Darshini Trivedi*

A group of 18 rising seniors from Duke University's Summer Undergraduate Fellowship program and their three graduate student mentors learned about environmental health science during a visit to NIEHS June 18. The students are participants in the National Science Foundation-funded [Chemistry Research Experience for Undergraduates](#) hosted by Duke's Chemistry Department.

Organized by NIEHS Office of Science Education and Diversity specialists John Schelp and Ericka Reid, Ph.D., the two-hour program of classroom instruction, a tour of NIEHS, and a visit to a research laboratory was one of the several outreach efforts conducted by NIEHS this summer for students at area colleges and universities.

## Introduction to resources and research at NIEHS

The program began with an overview of the NIEHS Summer Internship Program (SIP) by coordinator Debbie Wilson. Wilson described SIP as a mentoring internship and said the 8-12 week paid internship offers high school and college students a great opportunity for gaining hands-on experience in a research laboratory. During her talk, Wilson also emphasized the importance of a good cover letter and how critical it is to the application process.

Wilson's presentation was followed by a 45-minute overview of NIEHS by Michael Humble, Ph.D., a health scientist administrator in the NIEHS Cellular, Organ, and Systems Pathobiology Branch. Humble started off by giving the students a brief description of the 27 institutes that comprise the NIH and examples of the types of research conducted at the different institutes.

Humble then talked in detail about NIEHS and its vision "to prevent disease and improve human health by using environmental sciences to understand human biology and human disease," along with the four main components of the vision — basic research, human health and disease, global environmental health, and training. Amongst the variety of research conducted as part of global environmental health, Humble mentioned the GuLF (Gulf Long-term Follow-up) STUDY and the efforts of NIEHS scientists to study the long-term effects of the oil spill on the cleanup workers and volunteers.

## A hands-on tour of an NIEHS lab

The students then joined Schelp for a walking tour of the Institute. While standing in the lobby in front of Rodbell auditorium, Schelp acknowledged many of the famous scientists from NIEHS, including Nobel laureate Martin Rodbell, Ph.D., and described in



*Schelp quickly developed a rapport with his guests and clearly enjoyed his role as host and guide. (Photo courtesy of Steve McCaw)*



*As she described the summer internship experience, Wilson also offered practical advice on finding the right fit for the internship experience. (Photo courtesy of Steve McCaw)*



simple terms his award-winning research on how cells communicate. Schelp also described NIEHS/ NTP Director Linda Birnbaum, Ph.D., as being “very passionate about environmental health.”

Wendy Jefferson, Ph.D., a biologist in the Reproductive Medicine Group, gave the students a tour of her laboratory and talked about the research that her lab group conducts on studying the effect of the environment on reproduction and development. Jefferson talked about one of her favorite projects studying the effects of the phytoestrogen genestein on the reproductive status of mice.

As Jefferson told the students, phytoestrogens are naturally occurring plant steroids found in many consumable products, such as baby food, and high exposures of these compounds may have adverse effects on reproduction and development. She also discussed the various stages in embryonic development, including morula, blastula, and gastrula, and gave the students an opportunity to observe an early mouse embryo at the 4-cell stage of development, under a microscope.

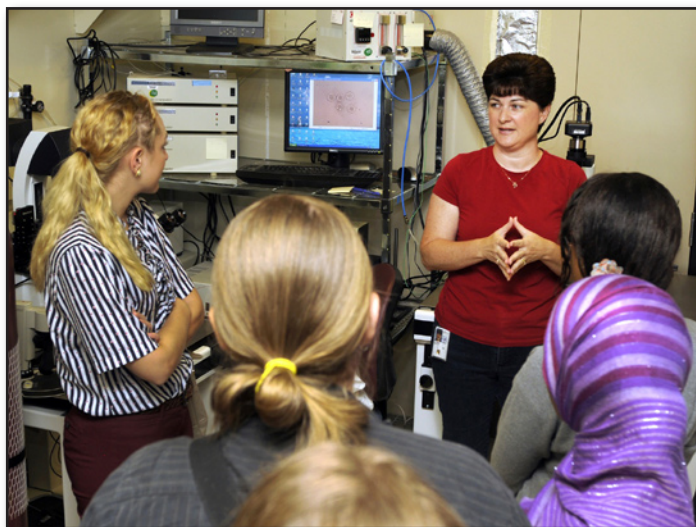
Asked about their overall thoughts on the tour, one of the students said enthusiastically, “I loved learning about all the research going on here. It is all very interesting.” The students found the tour very informative and thought NIEHS seemed to be a “nice place to work.”

(Darshini Trivedi, Ph.D., is a postdoctoral fellow in the NIEHS Metabolism and Molecular Mechanisms Group.)

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*Along with an introduction to NIEHS, Humble talked about his own experience in the Institute's Summer Internship Program and how it helped him decide to get his doctorate in toxicology. (Photo courtesy of Steve McCaw)*



*Jefferson, right, shared her passion for endocrine disruption research with students gathered in her lab. (Photo courtesy of Steve McCaw)*



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